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INSTITUTO DE CIÊNCIAS BIOMÉDICAS ABEL SALAZAR
UNIVERSIDADE DO PORTO

REABILITAÇÃO COGNITIVA ATRAVÉS DE AMBIENTES VIRTUAIS: INOVAÇÕES METODOLÓGICAS E TECNOLÓGICAS

ARTEMISA AGOSTINHA MONTEIRO DA ROCHA DORES

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Tese de Candidatura ao grau de Doutor em Ciências Biomédicas submetida ao Instituto de Ciências Biomédicas Abel Salazar da Universidade do Porto.

Orientador – Professor Doutor Alexandre Castro Caldas

Categoria – Professor Catedrático

Afiliação – Instituto de Ciências da Saúde da Universidade Católica Portuguesa.

Coorientador - Professora Doutora Liliana de Sousa

Categoria – Professora Associada

Afiliação – Instituto de Ciências Biomédicas Abel Salazar da Universidade do Porto.

Nesta introdução à perda de identidade que um transtorno do cérebro tinha acabado de desencadear, o que me parece desde logo implacável e irreversível é a precisão com que em tão rápido espaço de tempo fui desapossado das minhas relações com o mundo e comigo próprio.

José Cardoso Pires

Beneath the serene quiet of the water lilies
a young carp senses a calling . . . swelling up in her heart
like the swirling waters at the base of a great waterfall,
Somehow summoned to go beyond the barrier
of crashing water and veiled mist
The churning waters of the waterfall's bottom
matches that of the young carp's desires.

Finally with a burst of enthusiasm the carp has launched herself
up the wall of rushing water
cresting the first falls with a surge of effort
only to be met with relentless rushing water.
Persevering from one cataract to the next
the carp makes it to the summit's last falls.
Regrouping her energies in a pocket of scouring effervescence
every essence of strength, courage, and spirit is consumed
in the launching over the fall's summit.

And the dragon's gate accepts her efforts a transforming gate of fire
Revealing the birth of a new Dragon
born of the seed of desire planted in the heart of a small carp
that once hid in the shallows.

Howard Schroeder

Aos que me habitam,

Aos que fazem parte do que sou.

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Publicações

Na presente tese incluem-se resultados que foram alvo de publicação ou submetidos para publicação em colaboração com diversos autores como abaixo se discriminam.

O autor da presente tese declara serem da sua responsabilidade a conceção e execução do trabalho experimental, a análise e discussão dos resultados, a redação e submissão dos manuscritos publicados ou enviados para publicação.

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Lista de Abreviaturas, Acrónimos e Siglas

ABI – *Acquired Brain Injury*

AVE - Acidente Vascular Encefálico

CARP-VR – *Computer-Assisted Rehabilitation Program – Virtual Reality*

CRPG - Centro de Reabilitação Profissional de Gaia

EBIQ - *European Brain Injury Questionnaire*

ESTG – Escola Superior de Tecnologia e Gestão

EF – *Executive Functions*

ESTSP-PP - Escola Superior de Tecnologia da Saúde do Porto, Politécnico do Porto

FCUP - Faculdade de Ciências da Universidado do Porto

FEs – Funções Executivas

FEUP - Faculdade de Engenharia da Universidade do Porto

FMUP – Faculdade de Medicina da Universidade do Porto

HMD - *Head Mounted Display*

ICBAS - Instituto de Ciências Biomédicas Abel Salazar

ICS – Instituto de Ciências da Saúde

INESC-Porto - INstituto de Engenharia de Sistemas e Computadores do Porto

IPATIMUP - Instituto de Patologia e Imunologia Molecular da Universidade do Porto

IPVC - Instituto Politécnico de Viana do Castelo

ISEP - Instituto Superior de Engenharia do Porto

JG – Jogos Sérios

LCA – Lesão Cereral Adquirida

NECG – Núcleo Estudantil de Computação Gráfica

QOLIBRI - *Quality Of Live after Brain Injury*

RMf - Ressonância Magnética funcional

RV – Realidade Virtual

SG – *Serious Games*

SMIC - Serviço Médico de Imagem Computorizada

TBI – *Traumatic Brain injury*

TCE - Traumatismo Crânio-Encefálico

UCP – Universidade Católica Portuguesa

UP – Universidade do Porto

VR – *Virtual Reality*

WAIS-III - *Wechsler Adult Intelligence Scale-III*

WCST - *Wisconsin Card Sorting Test*

WMS - *Wechsler Memory Scale*

WHOQOL-BREF - *World Health Organization Quality of Life*

Resumo

A reabilitação neurocognitiva de pessoas com lesão cerebral adquirida (LCA) assume um interesse crescente, dado o aumento da incidência e da possibilidade de sobreviver após a sua ocorrência, frequentemente com défices físicos e cognitivos, bem como alterações afetivas e comportamentais. Uma das consequências mais comuns é a disfunção executiva, podendo ficar seriamente comprometidas capacidades importantes para a adaptação do comportamento no dia a dia, nomeadamente a iniciação, o planeamento, a sequenciação, a organização e a regulação do comportamento, suscitando a necessidade de intervenções inovadoras. A utilização de Jogos Sérios e da Realidade Virtual (RV) no domínio da reabilitação tem crescido de forma significativa nos últimos anos. Esta tecnologia oferece a oportunidade de desenvolver novos produtos, que podem ser utilizados na avaliação e na reabilitação neurocognitiva, e pode aumentar a sua validade ecológica. No entanto, importa investigar a sua aplicabilidade e a sua eficácia. O principal objetivo deste projeto é estudar a utilização dos Jogos Sérios e da RV na reabilitação da disfunção executiva e de funções subsidiárias, e os mecanismos cerebrais subjacentes à utilização desta tecnologia em tarefas específicas. Para tal, apresentamos um conjunto de 12 artigos, organizados em Enquadramento Teórico (dois artigos), Desenvolvimento, Implementação e Avaliação do *Computer-Assisted Rehabilitation Program - Virtual Reality* (CARP-VR) (cinco artigos), Desenho e Validação de Paradigmas Experimentais que permitam o estudo do substrato neuroanatómico envolvido no desempenho das tarefas do CARP-VR, através de ressonância magnética funcional (RMf) (quatro estudos) e em Trabalhos em Curso, a apresentação da continuidade dos trabalhos de desenvolvimento do CARP-VR (um artigo). A revisão da literatura evidencia a atualidade do tema e a necessidade de investigação adicional. Os resultados da implementação da versão atual do CARP-VR são promissores, suportando a usabilidade do Programa e a sua relevância na promoção da motivação para o processo de reabilitação. Os estudos de neuroimagem desenvolvidos sugerem que estímulos 3D, quando utilizados como “blocos de construção” em ambientes virtuais, podem induzir respostas emocionais de maior intensidade do que estímulos 2D. Também se encontrou uma interação do modo de visualização com a valência em áreas responsáveis pelo processamento emocional. A influência do 3D é igualmente encontrada no processamento visual, independente da valência emocional dos estímulos, suscitando maior ativação de certas áreas envolvidas no processamento visual. Em suma, os dados comportamentais obtidos com o CARP-VR sugerem vantagens da sua utilização e os estudos de neuroimagem indiciam que os materiais e tarefas utilizados são válidos para a avaliação e/ou reabilitação das funções visadas, na medida em que induziram a ativação de áreas cerebrais reconhecidas como parte do substrato neuronal associado a essas funções e permitiram a discriminação entre os grupos, saudável e com LCA. A finalizar esta tese, apresenta-se uma síntese integradora dos estudos acima descritos, discutindo resultados, limitações e perspetivas futuras. Com este projeto esperamos ter proporcionado um contributo válido na exploração do potencial da tecnologia RV no domínio da reabilitação, que aqui se demonstra, e na compreensão dos mecanismos cerebrais envolvidos nas tarefas propostas.

Palavras-chave: Reabilitação Neurocognitiva, Realidade Virtual, Jogos Sérios, Funções Executivas, Memória, Atenção, RMf.

Abstract

Neurocognitive rehabilitation of people with acquired brain injury (ABI) has gained increased interest, given the growing incidence of this type of injury and the possibility of survival, often with physical and cognitive deficits, as well as emotional and behavioral changes, after its occurrence. One of the most common consequences of ABI is executive dysfunction, which may seriously jeopardize important capacities for behavior adaptation in day-to-day life, including behavior initiation, planning, sequencing, organization and regulation. This calls for the need of innovative interventions targeted at this problem. The use of Serious Games and Virtual Reality (VR) in the field of rehabilitation has grown significantly in recent years. This technology provides the opportunity to develop new products that can be used in evaluation and neurocognitive rehabilitation practices, increasing the ecological validity of the instruments in this area. However, it is important to investigate the applicability and effectiveness of these products. The objective of this project is twofold: to study the use of Serious Games and of VR in the rehabilitation of executive dysfunction and subsidiary functions, and to inspect the brain mechanisms underlying the use of this technology in specific tasks. Within the scope of this project, we present 12 articles organized into: Theoretical Framework (two articles), Development, Implementation and Evaluation of a *Computer-Assisted Rehabilitation Program - Virtual Reality* (CARP-VR) (five articles), Design and Validation of Experimental Paradigms allowing the study of the neuroanatomical substrate involved in carrying out CARP-VR tasks through functional magnetic resonance imaging (fMRI) (four studies) and Work in Progress, the continuity of the development of CARP-VR (one article). The literature review shows that these themes are topical and need further investigation. The results of the implementation of the current version of CARP-VR are promising, supporting the usability of the program and its relevance in promoting motivation for the rehabilitation process. Neuroimaging studies suggest that 3D stimuli, when used as "building blocks" in virtual environments, can induce more intense emotional responses than 2D stimuli. The effect of an interaction between visualization type and valence in areas responsible for emotional processing was also found. The influence of 3D is also observed in the increased activation of certain brain areas of visual processing, regardless of the emotional valence of the stimuli. In short, the behavioral data obtained with CARP-VR suggest advantages to its use, and neuroimaging studies indicate that the materials and tasks employed are useful for evaluation and/or rehabilitation of the referred functions, since they induced the activation of brain areas recognized as part of the neuronal substrate associated with these functions and allowed the discrimination between (healthy and ABI) groups. To conclude this thesis, we present an integrative synthesis of the

above-mentioned studies, discussing their results, limitations and future prospects. With this project we expect to have provided a valuable contribution to exploring the potential of VR technology in the field of rehabilitation, shown here, and to the understanding of the brain mechanisms involved in the proposed tasks.

Keywords: Neurocognitive Rehabilitation, Virtual Reality, Serious Games, Executive Functions, Memory, Attention, fMRI.

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Introdução

As lesões cerebrais adquiridas (LCAs) em resultado de traumatismos crânio-encefálicos (TCEs) e de doenças neurológicas, como os acidentes vasculares encefálicos (AVEs), são uma das principais causas de morte e incapacidade em Portugal e noutros países industrializados (Bruns & Hauser, 2003; Coronado, Thurman, Greenspan, & Weissman, 2009; Coronado et al., 2011; INE, 2000; Martin, Lu, Helmick, French, & Warden, 2008; Mathers, Lopez, & Murray, 2001; Santos, de Sousa, & Castro-Caldas, 2003; WHO, 2002). Devido aos avanços na tecnologia médica e nos serviços de emergência, a mortalidade relacionada com estas causas diminuiu (Coronado, et al., 2011; INE, 2000; Santos, et al., 2003). Este facto, associado à sua ocorrência típica em jovens adultos, particularmente no caso dos TCEs (Coronado et al., 2011; Santos, de Sousa, & Castro-Caldas, 2003), resulta comummente em alterações físicas, comportamentais, emocionais e cognitivas, traduzindo mecanismos cerebrais afetados.

Défices cognitivos no domínio da atenção, da memória e das funções executivas comprometem frequentemente a capacidade de resolução de problemas quotidianos e de realização das mais básicas atividades de vida diária (Lewis, Babbage, & Leathem, 2011). Destes défices podem resultar decréscimos acentuados na qualidade de vida dos doentes[3] e das suas famílias, com documentadas implicações para a sua integração comunitária (Cernich, Kurtz, Mordecai, & Ryan, 2010; Chevignard, Brooks, & Truelle, 2010; Matheson, 2010). No caso de comprometimento das funções executivas, deslocar-se de modo independente ou realizar compras num supermercado podem ser atividades impossíveis. A utilização independente de transportes é mesmo considerada uma área nuclear na integração comunitária de indivíduos com incapacidade (Newbigging & Laskey, 1996). Contudo, para esta população, por motivos intrínsecos e extrínsecos, as possibilidades de contacto direto com a realidade social encontram-se o mais das vezes bastante limitadas. Além das suas próprias dificuldades, os obstáculos arquitetónicos e as alternativas existentes em termos de serviços não permitem atividades de participação social, com a variedade e a frequência desejáveis (Sohlberg, Todis, Fickas, Hung, & Lemoncello, 2005).

A tecnologia de Realidade Virtual (RV) apresenta-se como uma alternativa viável e promissora de aproximação ao real. Características como a possibilidade de *imersão* do utilizador num mundo percetivo gerado por computador, criando a sensação de que se está realmente nesse mundo (*presença*), a *interação* com o ambiente em tempo real, e o *envolvimento* do utilizador na tarefa, i.e., o seu investimento motivacional, conferem-lhe

[3] Será utilizado o conceito de “doente” por economia de linguagem.

um potencial inédito em diversas áreas, entre elas, a da saúde (Coelho, Tichon, Hine, Wallis, & Riva, 2006; Slater, Perez-Marcos, Ehrsson, & Sanchez-Vives, 2009).

A sua aplicação à reabilitação neurocognitiva oferece, hoje, a possibilidade de desenvolver novos programas que forneçam um ambiente protegido aos doentes, que possibilitem ultrapassar dificuldades colocadas por contextos reais e algumas das limitações dos programas tradicionais (como ausência de ligação com a experiência dos doentes), adequando simultaneamente os exercícios e ambientes à realidade da pessoa (customização). A aproximação da RV às condições dos contextos reais pode contribuir para aumentar o grau de generalização das competências desenvolvidas no âmbito de um programa, para situações da vida real (Dores et al., 2011, Guerreiro, Almeida, & Castro Caldas, 2008; Klinger, Chemin, Lebreton, & Marie, 2006; Koenig, Crucian, Dalrymple-Alford, & Duenser, 2009) – grau de generalização esse que é notoriamente baixo em programas de reabilitação neurocognitiva tradicionais (Calleo et al., 2012; Chevignard, et al., 2010). O recurso à RV apresenta ainda outras vantagens, umas únicas, noutros casos partilhadas com programas de treino cognitivo em suporte informático. Entre essas vantagens contam-se permitir o auto treino, programar o grau de dificuldade das tarefas em função da avaliação dos doentes, da sua evolução ou de modo contingente ao sucesso, fornecer *feedback* imediato, possibilitar a intervenção do terapeuta de modo a fornecer mais orientações ou a reabilitação à distância e a utilização de fatores de jogo para promover a motivação (Dores, et al., 2011; Riener, Luenenberger, & Colombo, 2006; Rizzo, Buckwalter, & Neumann, 1997; Rizzo & Kim, 2005; Rizzo, Strickland, & Bouchard, 2004; Schultheis & Mourant, 2001).

O recurso a esta tecnologia apresenta-se também como uma possibilidade na investigação científica de fenómenos de difícil reprodução em ambiente laboratorial e real, como as emoções (Riva et al., 2007; Wiederhold & Rizzo, 2005). Nos últimos anos aumentaram os estudos que aprofundam a avaliação dos diferentes sistemas da resposta emocional (Lang, Bradley, & Cuthbert, 1999), incluindo no que respeita ao seu substrato neurofisiológico (LeDoux, 2003), à sua influência sobre distintos processos cognitivos, como a memória (Ochsner & Schacter, 2000), a atenção (Lang, Bradley, & Cuthbert, 1997) ou a tomada de decisão (Damásio, 1994) e ainda ao défice do reconhecimento emocional em diferentes quadros de diagnóstico, como a LCA (Bornhofen & McDonald, 2008; Braun, Traue, Frisch, Deighton, & Kessler, 2005; Green, Turner, & Thompson, 2004), demonstrando a importância das emoções e da relevância de investigação nesta área. Mais especificamente, o reconhecimento de que a interpretação correta das emoções dos nossos interlocutores é fundamental para o sucesso das interações sociais e de que esta capacidade se encontra frequentemente comprometida na LCA suscita a necessidade de programas de reabilitação que considerem a intervenção nesta área.

Grande parte dos estudos atrás referidos utilizou como paradigma de investigação a visualização de imagens de conteúdo afetivo em contextos de experimentação laboratorial. Porém, a investigação dos fenómenos emocionais e a reabilitação da capacidade do seu reconhecimento com recurso à simples apresentação de diapositivos que contêm desenhos, palavras ou imagens, não facilita a sensação de presença no ambiente, nem a proximidade do estímulo indutor da emoção, logo, caracteriza-se por uma validade ecológica limitada que importa melhorar. A tridimensionalidade e a animação desses estímulos poderia facilitar a tarefa, ao tornar a expressão das emoções mais realista (Monteiro, Barbosa, & Silvério, in press).

Mais recentemente os Jogos Sérios (JS) têm beneficiado da tecnologia de RV (Perry et al., 2011). Este conceito surgiu na década de 90, traduzindo a intenção de aplicar os jogos a outras áreas que não a do lazer, e a fins que não o entretenimento em si mesmo, mas como um meio para atingir um fim específico, como por exemplo, a aprendizagem. Uma das áreas que tem explorado e começado a beneficiar com a sua aplicação é a da saúde (Chen & Michael, 2006; Zyda, 2005). No entanto, à semelhança do que se verifica com a RV, revela-se necessária investigação adicional acerca dos efeitos da aplicação dos JS à saúde em geral e na área da reabilitação em particular (Ma & Bechkoum, 2009; Ma et al., 2007).

Atendendo ao impacto que as LCAs podem ter, intervenções de reabilitação que permitam o retorno à vida ativa e devolvam qualidade de vida a estes doentes revelam-se cruciais (Zorowitz & Brainin, 2011). Desenvolver programas de reabilitação neurocognitiva inovadores e conhecer o substrato neuronal implicado neste processo, particularmente se envolve o recurso a tecnologias inovadoras e ainda pouco exploradas, como a RV, representam contribuições significativas para a investigação e para a prática nesta área. O melhor conhecimento do funcionamento cerebral envolvido nos programas com recurso a essa tecnologia contribuirá para melhorar os programas de intervenção.

Com a realização deste trabalho de investigação visámos estudar a utilização dos JS e da tecnologia de RV na reabilitação neuropsicológica, em particular das funções executivas e de funções subsidiárias, como as funções visuoespaciais, a atenção e a memória, pela relevância de que se revestem na reintegração da pessoa com LCA. Além dos potenciais benefícios destas tecnologias para a reabilitação, foi ainda nosso propósito estudar os mecanismos cerebrais envolvidos na realização de tarefas similares às que compõem o programa, investigados para assegurar que eram correlatos das funções mentais visadas ou, posto pela maneira inversa, para garantir que a intervenção atuava não apenas no comportamento, mas também no cérebro.

Para a prossecução do primeiro objetivo procedemos ao desenho, desenvolvimento, implementação e avaliação de um programa de reabilitação neurocognitiva com recurso à RV, o *Computer-Assisted Rehabilitation Program - Virtual Reality* (CARP-VR).[4] Com o seu desenvolvimento pretendemos inovar ao nível das práticas tradicionais, trazendo maior realismo, interação e envolvimento aos exercícios de reabilitação e maior eficácia e flexibilidade ao planeamento das intervenções. Este Programa dispõe de ambientes virtuais que permitem, em condições de segurança, resolver tarefas de vida diária (e.g., compras num supermercado), recorrendo a estratégias de reabilitação neurocognitiva teoricamente fundamentadas. Ao disponibilizar contextos interativos, próximos dos de vida real, visamos promover a superação ou diminuição das disfunções causadas por LCA e contribuir para aumentar a motivação para as tarefas de reabilitação (cf. Anexo I). Em última instância, com a utilização destes contextos de reabilitação virtuais procuramos favorecer a generalização das competências adquiridas aos ambientes reais, no sentido de potenciar a máxima funcionalidade e qualidade de vida dos doentes.

Para a prossecução do segundo objetivo deste projeto, a compreensão dos mecanismos cerebrais envolvidos, realizámos investigação com recurso a uma técnica de neuroimagem, a ressonância magnética funcional (RMf). Por ser uma técnica pouco invasiva, além das suas reconhecidas aplicações clínicas, começou a ser utilizada no domínio da investigação, permitindo o mapeamento das áreas cerebrais envolvidas nos diferentes processos cognitivos em indivíduos saudáveis. Ao combinar informação anatómica e fisiológica, com quantificação da hemodinâmica cerebral no decurso de uma atividade cognitiva, permite identificar a importância das diversas estruturas cerebrais para a atividade mental em curso (Baert, Sartor, & Youker, 2000; Brannen et al., 2001; Cravo, Palma, Conceição, & Evangelista, 2001). Porém, a sua utilização apresenta um conjunto de dificuldades, como a necessidade de seleção adequada da tarefa específica às áreas a ativar ou às operações cognitivas com elas relacionadas, a dificuldade de controlo de tarefas complexas realizadas em silêncio, a limitação do tempo para a realização das provas, a situação clínica do doente e, ainda, as distorções anatómicas no caso de lesões cerebrais (Sunaert & Yousry, 2001).

Pelas dificuldades enunciadas, percebe-se que o recurso à RMf com vista à compreensão dos mecanismos cerebrais envolvidos no processo de reabilitação, designadamente quando esse processo envolve RV e JS, apesar da sua relevância extraordinária na validação biológica e na melhoria dos programas de reabilitação, não é um propósito de fácil alcance. Procurando contribuir para esta área, dedicámo-nos à exploração do efeito da tridimensionalidade (3D) no funcionamento cerebral, por ser uma

[4] O acrónimo e o logotipo escolhidos simbolizam as capacidades de coragem e perseverança na superação de obstáculos associadas à carpa na mitologia oriental. Remetem para a metáfora da necessidade de se trabalhar árdua e diligentemente para se alcançar a mudança pretendida. É ao serviço desse processo de mudança, subjacente à reabilitação neuropsicológica de modo global, que pretendemos colocar o CARP-VR (cf. Anexo I – Manual do Programa)

característica distintiva da RV. Pretendemos ainda estudar o efeito do conteúdo emocional dos estímulos. Esperávamos identificar ativações diferenciais em áreas do cérebro relacionadas com o processamento de estímulos visuais emocionógenos de valência agradável ou desagradável e, simultaneamente, verificar se os padrões de ativação neuronal eram influenciados pela tridimensionalidade dos estímulos. Demos ênfase diferenciada a cada uma destas variáveis (valência emocional e modo de visualização, 2D *vs* 3D), nos dois estudos realizados neste âmbito. Ainda no domínio da neuroimagem funcional, propusemo-nos desenvolver e validar novos estímulos e paradigmas metodológicos, explorando as redes neuronais ativadas por tarefas de controlo atencional e inibitório e por tarefas de memória de trabalho, pela estreita relação que apresentam com as funções executivas, que pretendemos continuar a estudar em populações clínicas.

Em suma, não se pretendendo minimizar o valor do trabalho atualmente realizado no domínio da reabilitação, até porque há vastas evidências da sua eficácia (Cicerone et al., 2005; Cicerone et al., 2011; Koehler, Wilhelm, & Shoulson, 2011), a sua combinação com as evoluções tecnológicas que têm emergido é potencialmente otimizadora dessa eficácia, pelas razões que acima se explicitaram, permitindo também inovar nas práticas e rentabilizar os recursos. Atendendo à relevância do tema e porque, tanto quanto se sabe, os estudos desta natureza são escassos na comunidade científica internacional e inexistentes no nosso país (cf. Artigos 1 e 2), propusemo-nos desenvolver o trabalho de investigação documentado nesta tese de doutoramento.

Tomando como quadro de referência os problemas atrás enunciados e as limitações que os programas de reabilitação convencionais parecem apresentar para os resolver de forma satisfatória, os nossos trabalhos foram presididos pelas seguintes questões gerais de investigação:

1. Qual a atual aplicação da RV na reabilitação e que provas existem sobre a sua eficácia?
2. Qual a importância das funções executivas na reintegração da pessoa com LCA, de que modo é conceptualizado esse funcionamento e quais as práticas atuais de intervenção e investigação sobre este objeto?
3. Como organizar o processo de desenvolvimento de um programa de reabilitação neurocognitiva com recurso à tecnologia de RV? Qual(ais) o(s) modelo(s) a seguir?
4. Quais as funcionalidades que deve ter um programa de reabilitação neurocognitiva das funções executivas e de outras funções subsidiárias e quais as soluções tecnológicas e informáticas que permitem a sua concretização?
5. Como responder à necessidade de programas de reabilitação neurocognitiva que permitam a fácil adequação das suas características, designadamente em termos de

cenários, permitindo uma maior aproximação ao real e que não constituam uma barreira à participação?

6. Como inovar as práticas de reabilitação neurocognitva atuais, através do recurso aos JS e à RV? Podem os programas desenvolvidos adequar-se ao desempenho atual do sujeito e pode tal ser realizado pelo terapeuta, sem conhecimentos de programação?

7. Qual a evidência da eficácia dos JS e da RV na reabilitação neurocognitiva? Como avaliar a usabilidade e os efeitos no comportamento de um programa desenvolvido com recurso a estas tecnologias? É a tridimensionalidade uma característica da RV valorizada pelos doentes utilizadores do CARP-VR?

8. Qual o efeito da tridimensionalidade, como característica da RV, nas respostas emocionais? Como avaliar esta variável?

9. Qual o efeito da tridimensionalidade, como característica da RV, não só nas respostas emocionais, como também no processamento visual? Pode a valência emocional moderar este efeito? Como avaliar estas variáveis?

10. Como estudar o impacto da participação em JS de reabilitação neurocognitiva das funções executivas no funcionamento cerebral? Qual(ais) as tarefas a utilizar para avaliar e/ou reabilitar o controlo atencional e inibitório como componentes das funções executivas?

11. E qual(ais) as tarefas a utilizar para avaliar e/ou reabilitar a memória de trabalho, como componente de avaliação das próprias funções executivas?

12. Está um programa de reabilitação neurocognitiva concluído com a concretização das especificações iniciais ou beneficia de atualizações decorrentes de avanços teóricos e tecnológicos? Quais as principais limitações na reabilitação das funções executivas, não colmatadas pelos programas atualmente existentes?

Para dar resposta a estas questões, organizaram-se um conjunto de estudos interdependentes, de cujos objetivos específicos e produtos científicos deles decorrentes se dará conta, de forma abreviada, mais adiante. De modo genérico, os estudos encontram-se estruturados em *Enquadramento Teórico* (Artigos 1 e 2), *Desenvolvimento, Implementação e Avaliação do Computer-Assisted Rehabilitation Program - Virtual Reality* (CARP-VR) (Artigos 3 a 7), Desenho e Validação de Paradigmas Experimentais (Artigos 8 a 11) e *Trabalhos em Curso* (Artigo 12)[5].

I. Enquadramento Teórico

Artigo 1. Realidade Virtual na Reabilitação: Por que Sim e Por que Não?

Neste estudo de revisão sistemática da literatura pretendemos analisar a produção científica relacionada com a RV aplicada ao domínio da reabilitação. Da sua realização,

[5] Por uma questão de uniformização do estilo não se apresentam os PDFs dos artigos originais ou submetidos, mas mantêm-se na íntegra: o texto original, a língua em que os artigos foram publicados/submitidos e o estilo das referências, com exceção do Artigo 12, que foi publicado nuima versão mais reduzida.

resultou o desenvolvimento e a apresentação de um modelo que permitisse, de modo hierarquizado, descrever e sistematizar a natureza dos estudos revistos, as principais temáticas abordadas e as suas conexões, com especial realce para o contributo da RV no domínio da reabilitação neuropsicológica.

Artigo 2. Conceptualizations and Rehabilitation in Executive Functions: A Systematic Literature Review.

Nesta segunda revisão procurámos explorar a diversidade em torno das funções executivas, desde a sua conceptualização aos efeitos da sua disfunção, passando pelas práticas de avaliação e reabilitação e pelos correlatos neuroanatómicos. Da sua realização obteve-se e propôs-se uma visão integradora acerca deste objeto, expressa no modelo por nós proposto, sistematizando o conhecimento atual e sinalizando direções futuras para as práticas de intervenção e investigação.

II. Desenvolvimento, Implementação e Avaliação do *Computer-Assisted Rehabilitation Program - Virtual Reality* (CARP-VR)

Artigo 3. O Desenvolvimento de um Programa de Reabilitação Cognitiva com Recurso a Tecnologias Informáticas.

O processo de desenvolvimento de programas de reabilitação neurocognitiva com recurso a tecnologias informáticas e a equipas multi- e interdisciplinares revela-se exigente, e enfrenta desafios tais como, por vezes, o difícil equilíbrio entre a fundamentação teórica e a prática. Este processo merece reflexão e reclama a existência de modelos orientadores das práticas, que procurem conciliar de forma harmoniosa os contributos das diversas áreas necessárias à sua consecução, como a neuropsicologia ou a engenharia computacional. Deste trabalho resultou a proposta de um modelo orientador do processo de desenvolvimento de um programa de reabilitação neurocognitiva com recurso a tecnologias informáticas, fundamentado na literatura existente e na experiência adquirida pela equipa.

Artigo 4. *Virtual Reality: Application to Cognitive Rehabilitation after Acquired Brain Injury*.

Neste artigo e no seguinte tivemos como objetivo discutir o desenvolvimento do CARP-VR, desde o início do projeto e nos seus múltiplos progressos, junto da comunidade científica especializada, com o intuito de recolher contributos à sua melhoria. Deste debate e da testagem repetida do Programa, ao longo do processo, surgiram readaptações desejáveis à sua melhoria. Em concreto neste artigo, depois de um breve enquadramento teórico acerca da aplicação da RV à LCA, é apresentado o projeto CARP-VR.

Artigo 5. New Answers for Old Questions in the Domain of the Cognitive Rehabilitation.

Neste artigo, depois de introduzida a questão da reabilitação em Portugal e dos desafios que se colocam à sua realização neste contexto, são abordados dois dos desafios identificados: (1) a necessidade de programas flexíveis que possam ser adequados às especificidades dos doentes; e, (2) de programas multimodais que não se constituam como barreiras à sua participação. Resultou daqui a proposta de um editor de mapas que permitisse a manipulação dos ambientes virtuais, pelos terapeutas, de modo a criar cenários alternativos e a proposta de uma interface de voz facilitadora da participação de doentes com limitações físicas.

Artigo 6. Computer-Assisted Rehabilitation Program – Virtual Reality (CARP-VR): A Program for Cognitive Rehabilitation of Executive Dysfunction.

Neste artigo pretendemos fazer a apresentação oficial do CARP-VR, na sua versão final. Depois de uma breve revisão do estado da arte, o Programa é apresentado, bem como as suas funcionalidades, o racional e a tecnologia subjacente. Entre as funcionalidades, além do editor de mapas, é descrito o editor de níveis que permite ao terapeuta especificar as tarefas e o seu nível de dificuldade, caso decida não optar pelos níveis pré-definidos (cf. Anexo I – Manual do Programa).

Artigo 7. Serious Games: Are They Part of the Solution in the Domain of Cognitive Rehabilitation?

Neste trabalho visámos analisar as vantagens da utilização de JS na área da saúde e a possibilidade de receberem contributos da RV, decorrentes da sua utilização conjunta. Depois de uma revisão conceptual e de discutidas potenciais vantagens, são apresentados os resultados de três estudos em que se investiga: (1) a satisfação dos doentes com a participação no CARP-VR (versão inicial) e o seu desempenho nas tarefas do mesmo, utilizando o modo de visualização bidimensional (2D); (2) o mesmo com o modo de visualização tridimensional (3D); e, (3) a satisfação dos doentes com o Programa (versão final), ainda enquanto exemplo de um JS, a sua usabilidade e a motivação dos sujeitos para participar nas tarefas do programa.

III. Desenho e Validação de Paradigmas Experimentais

Artigo 8. Amygdalae Activation to 2D and 3D Emotional Inducing Stimuli.

Neste estudo tivemos como objetivo testar estímulos de maior realismo, resultado da utilização da tecnologia de RV, na indução de emoções em ambiente laboratorial controlado, onde são possíveis medidas neuroimagiológicas em tempo real. Foi também perceber se as respostas emocionais podem ser modeladas pela tridimensionalidade dos estímulos, visto essa característica potenciar a sensação de presença do sujeito nos ambientes virtuais. Os resultados sugerem que estímulos em 3D, quando utilizados como “blocos de construção” em ambientes virtuais, podem induzir respostas emocionais de maior intensidade do que estímulos em 2D.

Artigo 9. Effects of Emotional Valence and Three-dimensionality of Visual Stimuli on Brain Activation: an fMRI Study.

Devido ao potencial ecológico e à diversidade de aplicações da RV, neste estudo pretendemos explorar se uma das suas características distintivas, a tridimensionalidade, também estudada no Artigo 8, pode modular a atividade cerebral nas áreas responsáveis pelo processamento emocional e visual. Ainda perceber se a valência emocional (agradável, desagradável, neutra) pode moderar esse efeito. Verificou-se uma interação do modo de visualização (2D, 3D) com a valência emocional, tendo sido analisada a direção dos efeitos. Foi também encontrada a influência do modo de visualização em 3D, independendente da valência emocional, no processamento emocional e no processamento visual e clarificado o efeito da valência emocional, de modo independente do tipo de visualização, que sugere o impacto das emoções negativas.

Artigo 10. *An fMRI Paradigm Based on Williams Inhibition Test to Study the Neural Substrates of Attention and Inhibitory Control.*

Neste estudo e no seguinte visámos trazer contributos à investigação no domínio da neuroimagem funcional, pela validação de paradigmas que ajudem a superar dificuldades em torno da seleção adequada da tarefa específica às áreas a ativar ou às funções cognitivas que se pretende estudar, designadamente que permitam o estudo do substrato neuroanatómico envolvido no desempenho de tarefas do CARP-VR que configuram "pedras angulares" para o sucesso da reabilitação das funções executivas, como é o caso das que respeitam à atenção, controlo inibitório ou memória de trabalho. Como resultado este artigo apresenta um paradigma, com base no Williams Inhibition Test (WIT), para o estudo do controlo atencional e inibitório e do substrato neuroanatómico envolvido, através de dados funcionais e comportamentais.

Artigo 11. *Study of Behavioral and Neural Bases of Visual Working Memory with an fMRI Paradigm Based on a Visuospatial N-back Task.*

Atendendo ao exposto anteriormente (Artigo 10) no presente estudo tivemos como objetivo melhorar o conhecimento disponível sobre as bases neuronais e implicações comportamentais da memória de trabalho em participantes saudáveis. Neste sentido propusemos e validámos um paradigma de RMf utilizando uma adaptação da tarefa *n-back* de memória de trabalho, com material não verbal, a fim de evitar vieses culturais ou educacionais.

IV. Trabalhos em Curso

Artigo 12. *Virtual City: Neurocognitive Rehabilitation of Acquired Brain Injury.*

Neste artigo documentámos o trabalho em curso para dar continuidade ao desenvolvimento do CARP-VR. Desta tarefa resulta a apresentação do protótipo: Cidade Virtual, que consiste em ambientes virtuais urbanos que simulam cenários e atividades da vida real. Com a conclusão destes trabalhos o CARP-VR adquirirá novas funcionalidades, de que se dá conta neste artigo, como o aumento do número de ambientes disponíveis e de atividades de vida diária, a aplicação de um algoritmo à progressão entre níveis, tornando-a automática e contingente ao desempenho individual, e a possibilidade de realizar o Programa à distância, sob supervisão clínica (cf. Anexo II e III).

A finalizar esta tese, apresentámos uma síntese integradora dos estudos acima descritos e dos resultados alcançados, discutindo as suas principais conclusões no quadro das metodologias adotadas e as suas limitações, terminando com direções a prosseguir com a investigação neste domínio.

I. Enquadramento Teórico

Artigo 1 - Realidade Virtual na Reabilitação: Por que Sim e Por que Não? Uma Revisão Sistemática

Dores, A. R., Barbosa, F., Marques, A., Carvalho, I. P., de Sousa, L., & Castro-Caldas, A. (submetido). Realidade virtual na reabilitação: por que sim e por que não? Uma revisão sistemática.

Realidade virtual e reabilitação: por que sim e por que não? Uma revisão sistemática
Virtual reality and rehabilitation: why or why not? A systematic literature review

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Resumo

O processo de avaliação e de reabilitação neuropsicológica continua a ser um desafio para profissionais, pacientes e suas famílias. Procurando superar as limitações das intervenções tradicionais, a tecnologia de Realidade Virtual (RV) tem sido aplicada de forma crescente e começa a fornecer ferramentas neste domínio.

O presente estudo teve como objectivo analisar a produção científica até Novembro de 2010, relacionada com a RV aplicada ao domínio da reabilitação. Ainda desenvolver e apresentar um modelo que permite de modo hierarquizado, descrever e sistematizar a natureza dos estudos revistos, as principais temáticas abordadas e as suas conexões, com especial realce para o contributo da RV no domínio da reabilitação neuropsicológica.

Neste trabalho realizámos uma revisão sistemática da literatura de trabalhos científicos, indexados na base de dados ISI Web of Knowledge, utilizando a equação de pesquisa: ("Virtual Reality" OR "Virtual Environment") AND "Rehabilitation". Após uma breve introdução à realidade virtual, discutimos a metodologia e estratégia analítica (protocolo aplicado), e apresentamos os dados recolhidos. Foram identificados 963 artigos, dos quais 288 títulos e resumos foram analisados. O modelo desenvolvido identificou como categorias nucleares/centrais: Tipo de Artigo (Empírico; Teórico); Contextualização do Projecto; Tipo de Abordagem (Tecnologia Assistiva; Realidade Aumentada; Abordagens Tradicionais; Realidade Virtual). Esta última categoria foi decomposta de forma exaustiva, procurando documentar a sua aplicabilidade, impactos e tendências futuras.

Os resultados evidenciam tendências promissoras acerca da utilização da tecnologia de RV no domínio da reabilitação, com implicações para a forma como será realizada no futuro. Emerge ainda dos resultados, a necessidade de dar continuidade aos trabalhos que procuram avaliar a aplicabilidade da RV na reabilitação em geral e das funções executivas em particular.

Palavras-chave: Realidade virtual, Reabilitação, Revisão sistemática da literatura

Abstract

The process of neuropsychological assessment and rehabilitation remains a challenge for professionals, patients and their families. Seeking to overcome the limitations of traditional interventions, Virtual Reality (VR) technology has been applied in a growing way and begins to provide tools in this field.

This study aimed to analyze the scientific production by November 2010, related to the VR applied to the field of rehabilitation. Also develop and present a model that allows hierarchical order, describe and systematize the nature of the studies reviewed, the main issues addressed and their connections, with special emphasis on the contribution of VR in the field of neuropsychological rehabilitation.

In this work we conducted a systematic review of scientific papers indexed in the database ISI Web of Knowledge, research using the equation: ("Virtual Reality" OR "Virtual Environment") AND "Rehabilitation." After a brief introduction to VR, we discuss the methodology and analytical strategy (protocol applied), and present the data collected. 963 articles were identified of which 288 titles and abstracts were reviewed. The model categories identified as nuclear were: Type of Article (Empirical, Theoretical), Project´s Background; Approach Type (Assistive Technology, Augmented Reality; Traditional Approaches, Virtual Reality). This last category was decomposed thoroughly, seeking to document the VR´s applicability, impact and future trends.

The results show promising trends on the use of VR technology in the field of rehabilitation, with implications for how the future will be held. Also mention the results, the need to continue the work that seeks to evaluate their applicability in general and in the rehabilitation of executive functions in particular.

Keywords: Virtual reality, Rehabilitation, Systematic literature review

INTRODUÇÃO[6]

Assistimos hoje a um proliferar de publicações acerca da aplicabilidade da tecnologia de realidade virtual (RV), que transcendem o tradicional domínio do entretenimento, como o cinema, os jogos eletrónicos ou a publicidade, fonte quase exclusiva da sua aplicação durante as últimas décadas. Mesmo sendo considerada uma tecnologia recente, os primórdios da RV estão associados à indústria aeroespacial e de defesa americanas[1,2], aos trabalhos do cineasta Morton Heiling, na década de 60[3,4] e de Sutherland, reconhecido como o criador da RV[2,4]. Na década de 80, Jaron Lanier, contribuiu decisivamente para a popularização do termo RV e para a aplicação desta tecnologia a fins comerciais[5,6]. A maior facilidade de acesso à RV viria a desencadear renovações metodológicas em diversas áreas, na procura de soluções mais flexíveis e inovadoras.

O potencial desta tecnologia advém das suas principais características, designadamente a possibilidade de *imersão* do utilizador num mundo percetivo gerado por computador, ou seja, a emulação laboratorial da realidade e a sensação do sujeito de que lá está realmente (*presença*)[7,8], a possibilidade de *interação* com o ambiente em tempo real, conferindo ao sujeito um papel ativo, por exemplo, na exploração/navegação do ambiente, e o maior *envolvimento,* concebido como participação, atenção e persistência do utilizador na tarefa, isto é, o seu investimento motivacional.

Das áreas que se têm dedicado à aplicação da RV, destacamos a das Ciências da Saúde, onde tem sido utilizada na investigação, formação/educação, avaliação e intervenção terapêutica ou reabilitativa em diversos domínios. Enquanto instrumento de investigação permite a exposição do utilizador a ambientes virtuais que podem simular acontecimentos realmente vivenciados e, por exemplo, a monitorização e a avaliação objetiva, em tempo real, das suas reações psicofisiológicas[9,10]. Enquanto instrumento de formação/educação, permite o desenvolvimento de competências cruciais ao exercício profissional, passíveis de aquisição através de treino simulado (e.g., procedimentos cirúrgicos complexos)[11,12]. Por último, a sua utilização enquanto instrumento de avaliação e reabilitação ou tratamento permite ultrapassar limitações das ferramentas tradicionais, esperando-se que contribua para potenciar os efeitos das intervenções existentes e otimizar a sua eficiência. A título de exemplo, vários trabalhos publicados demonstram o interesse da RV na reabilitação motora[13], do equilíbrio e/ou marcha[14], ou no treino da manipulação de cadeiras de rodas[15], na reabilitação neurocognitiva de pessoas com traumatismos cranioencefálicos[16-18] ou, ainda, em vítimas de doenças cardiovasculares[19]. No domínio da saúde mental, a RV tem sido aplicada no tratamento das fobias,

[6] As referências bibliográficas deste artigo encontram-se no formato proposto pela revista a que foi submetido.

permitindo o confronto controlado dos doentes com as situações fóbicas[20] e na perturbação de stresse pós-traumático, viabilizando a exposição *in vivo* do paciente ao ambiente stressor, de forma gradual, prolongada e sistemática. Também no comportamento aditivo e em outras patologias do impulso[20,21], a RV pode ser utilizada como parte integrante de uma abordagem cognitivo-comportamental, proporcionando, através do condicionamento operante, a saciação da estimulação que mantém o comportamento aditivo. Conhecem-se igualmente aplicações nas perturbações de pânico[23], perturbações alimentares[24], perturbações do espectro do autismo[25], paralisia cerebral e síndrome de Down[26], perturbação da imagem corporal[27], doença de Parkinson[28], entre outras. Vários trabalhos têm também sido publicados relativamente ao papel da RV na avaliação[29], associados ao desenvolvimento de novos instrumentos de avaliação neuropsicológica ou à alteração de outros já existentes, de modos a torná-los mais ecológicos[30].

Presentemente, as soluções tecnológicas existentes (*head-mounted displays, eyeglasses,* entre outros) são cada vez mais diversas, acessíveis e de maior qualidade. Apesar disso, as aplicações científicas e clínicas da RV e o seu desenvolvimento implicam muito mais do que a disponibilidade da tecnologia. Do racional teórico subjacente ao desenho de métodos de investigação ou a programas de intervenção, aos estudos de validação da sua aplicabilidade, existe um longo percurso carente de sustentação empírica. Essa sustentação pode ser obtida por métodos diversos, como os que são próprios da neuropsicologia ou através de técnicas de neuroimagem funcional[33].

Em suma, das áreas anteriormente enunciadas a reabilitação continua a ser um desafio para profissionais, pacientes e suas famílias. Procurando superar as limitações das intervenções tradicionais, a RV tem sido aplicada de forma crescente e começa a fornecer importantes ferramentas neste domínio. Apesar disso, a possibilidade de o fazer não é unânime e requer clarificação. Reflexo da sua juventude, dimensões nucleares, como a terminologia a utilizar e a sua definição, ou as (des)vantagens da RV são ainda pouco consensuais, sendo objeto de debate frequente e de posicionamentos distintos ou mesmo contraditórios. No sentido de averiguar a pertinência do uso da RV na reabilitação, e assim fornecer informação que contribua para esclarecer pontos deste debate, este estudo debruça-se sobre a análise das vantagens e limitações desta tecnologia, procurando responder à questão: Realidade Virtual e Reabilitação: Por que sim e por que não?

Com este fim, foi desenvolvido um modelo hierarquizado que procura descrever e sistematizar a natureza dos trabalhos revistos, as principais temáticas abordadas e as suas interligações. Neste artigo, o modelo será apresentado sucintamente e a análise circunscrita à temática do presente trabalho, acima enunciada.

MATERIAL E MÉTODOS

Este é um trabalho estrutural que integra um estudo mais abrangente, com o objetivo de caracterizar a RV, o estado do conhecimento atual da sua aplicação ao domínio da reabilitação, e identificar questões relevantes da investigação neste domínio.

Procedimento

Foi realizada uma revisão sistemática dos documentos científicos indexados na base de dados *ISI Web of Knowledge*, desde o início até novembro de 2010, utilizando as palavras chave e a equação de pesquisa em linguagem Booleana: (“*virtual reality*” OR “*virtual environment*”) AND "*rehabilitation*". A escolha de termos nesta pesquisa deriva do conhecimento da literatura no domínio.

Foram identificados 963 artigos entre 1997 e novembro de 2010. Os critérios de exclusão foram áreas pouco relacionadas com a temática da pesquisa, como *operations research & management science; biochemistry & molecular biology; hematology; otorhinolaryngology; integrative & complementary medicine; microscopy; dermatology*, entre outras. Só foram considerados documentos redigidos em inglês e dos seguintes tipos*: abstracts, meeting* e *article review*. Depois da aplicação dos critérios de exclusão, obtivemos 288 documentos. Destes, foram excluídos 25 por não apresentarem resumo e três por serem repetidos. Dos 263 documentos retidos, foram analisados os títulos e os resumos. Estes documentos (Apêndice 1) foram exportados para o Endnote e os seus títulos e resumos novamente exportados para um projeto do NVivo.

Análise

A análise dos dados foi realizada por dois investigadores independentes e validada por um terceiro - juiz. O processo de análise de conteúdo com recurso ao NVivo foi conduzido em duas fases. A primeira foi de análise indutiva (sem categorias prévias) para identificar as categorias e subcategorias que melhor traduzem as temáticas expressas na literatura revista. Numa segunda fase, o modelo desenvolvido a partir da primeira fase foi aplicado à recodificação do material.

Assim, de modo detalhado, os dois investigadores realizaram codificação livre e construíram uma árvore hierarquizada com as (sub)categorias identificadas. O revisor 1 analisou a totalidade do material (263 títulos e resumos) e o revisor 2 analisou 100% do material até 2004 e 50% de cada um dos anos seguintes. As *unidades de registo* foram os *temas* (unidades de dimensões imprecisas mas que permitem perceber o contexto, conferindo maior significado à unidade de registo). A *unidade de enumeração ou contagem* foi o critério *todas as vezes que a unidade* (tema) *aparece*. Em resultado desta análise, os revisores construíram os seus modelos preliminares. Estes foram comparados, procurando-se consensos e pontos de dissonância. As alterações efetuadas consistiram, fundamentalmente, na uniformização da terminologia, na fusão de categorias secundárias e na reorganização de algumas ligações entre conceitos. O modelo final resultante deste acordo inter-revisores procura descrever o mais objetivamente possível a natureza e qualidade da informação analisada.

De modo a validar a codificação original, os dois revisores utilizaram o modelo desenvolvido para recodificar o material. A recodificação foi conduzida independentemente. Procurou-se, assim, testar a robustez e a validade interna da ferramenta previamente construída. O cálculo do acordo interpares utilizou o kappa de Cohen (de 0.81), por ser considerado uma medida mais robusta do que a simples percentagem de acordo.

RESULTADOS

Artigos por ano e autores mais frequentes

Na figura 1 podemos observar que o número de publicações aumentou consideravelmente ao longo dos últimos anos, sendo a exceção mais significativa o ano de 2008.

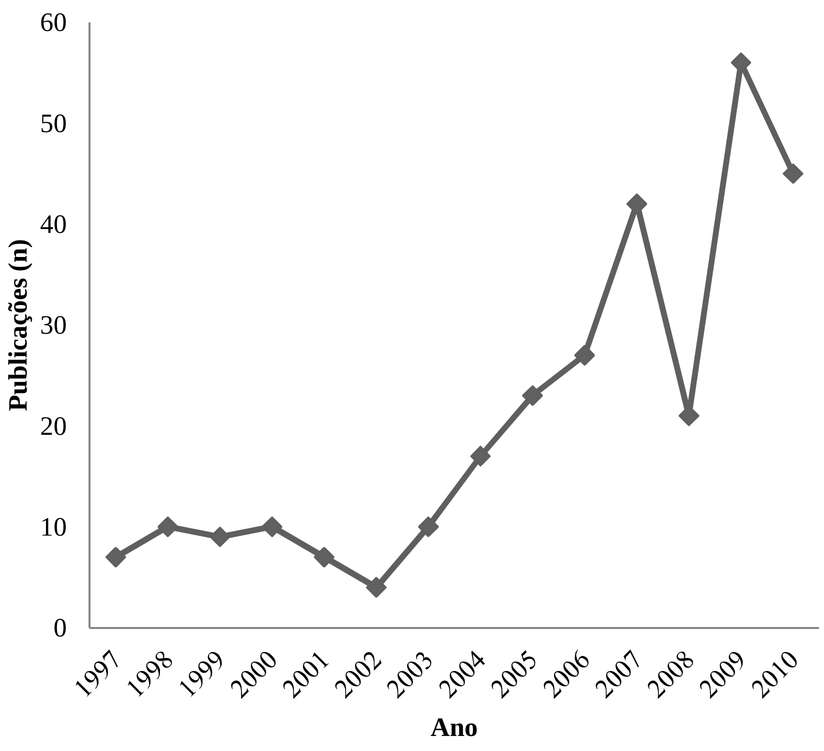

Figura 1 - Número de publicações por ano até outubro de 2010

O modelo desenvolvido identificou como categorias nucleares (de primeira e segunda ordem): *Tipo de Artigo* (*Empírico, Teórico*) e *Tipo de Abordagem* (*Tecnologia Assistiva, Realidade Aumentada, Abordagens Tradicionais, Realidade Virtual*). As várias categorias foram decompostas nas dimensões que mais emergiram da literatura, chegando, em alguns casos, a variáveis de sexto nível. Destas últimas, a RV foi decomposta de forma exaustiva (*Definição*, *Características*, *Aplicações*, *Fatores Humanos* implicados (e.g., *Questões Éticas*), *Produtos*, *Profissionais* envolvidos na sua utilização e *Investigação Futura*), nomeadamente em termos de *Vantagens* e *Limitações*, que constituem o âmbito deste trabalho e foram organizadas nas subcategorias a seguir identificadas.

Vantagens da RV surgiram relacionadas com:

a) **a possibilidade de aplicação a uma diversidade de domínios (e.g., medicina, neuropsicologia)**

Virtual reality environments have many potential applications in medicine, including surgical training, tele-operated robotic surgery, assessment and rehabilitation *of physical disabilities ….* **(Lewis et al., 1997)**
(…) The review concludes that the use of VR in brain damage rehabilitation is expanding dramatically and ***will become an integral part of cognitive assessment and rehabilitation in the future****.* **(Rose et al. 2005)**

b) **a possibilidade de aplicação a uma diversidade de funções cognitivas, comportamentos, doenças neurológicas e incapacidades físicas**

Virtual reality environments have many potential applications in (…) assessment and rehabilitation of ***behavioural and neurological disorders and diagnosis, therapy and rehabilitation of physical disabilities.*** **(Lewis et al., 1997)**
It is suggested that virtual reality can be used in MS patients to assess aspects of ***spatial memory*** *that are not measured by traditional tests.* **(Pugnetti et al., 1998)**
The results of this preliminary study indicate that training in virtual environments may prove an effective method of teaching new information to patients with ***severe memory impairments****.* **(Brooks et al., 1999)**
Enhanced feedback provided by a virtual reality system has been shown to promote ***motor learning*** *in normal subjects.* **(Piron et al., 2005)**
Virtual reality (VR) possesses many qualities that give it rehabilitative potential for people with ***intellectual disabilities****, both as an intervention and an assessment.* **(Standen et al., 2005)**
Since the VRET scenario was shown to be a robust tool in the reduction of ***fear of falling****, virtual reality technology is proposed as a promising platform for the development of such retraining applications.* **(Giotakos et al., 2007)**
Virtual reality systems have been used to deliver goal directed repetitive training to promote rehabilitation of individuals ***post-stroke****.* **(Mirelman et al., 2007)**
Those results will support the use of virtual reality for situated ***neglect*** *assessment and provide guidelines for rehabilitation trials in more ecologically-like contexts.* **(Morganti et al., 2007)**
Virtual reality (VR) has enormous potential as an adjunct in therapy. VR has many of the parameters shown to be effective in ***motor learning****.* **(Guberek et al., 2008)**
Adults with ***intellectual disabilities (ID) and physical disabilities*** *often experience limited opportunities to participate in leisure activities, virtual reality (VR) technologies may serve to broaden their repertoire of accessible* ***leisure activities****.* **(Yalon-Chamovitz et al., 2008)**
While rehabilitation approaches of the ***dysexecutive syndrome*** *are still limited, Virtual Reality (VR) has shown its potential to propose innovative intervention strategies based on ecologically valid functional tasks.* **(Klinger et al., 2009)**

To further promote generalization of gained abilities and to quantify functional improvements, this project aims at developing a Virtual Reality (VR) application that can be used for training and assessment of ***spatial orientation and navigation skills*** *in* ***brain-damaged patients****.* **(Koeniget al., 2009)**

There is potential for the use of VR and game applications for rehabilitating, maintaining, and enhancing those processes that are ***affected by aging*** *with and into disability, particularly the need to attain a balance in the interplay between* ***sensorimotor function and cognitive demands*** *and to reap the benefits of task-specific training and regular physical activity and exercise.* **(Lange et al., 2010)**

Thus, VR rehabilitation therapy can be effective in improving the ***physical dyskinesia*** *caused by* ***cerebrovascular disease*** *and the* ***daily living*** *skill of the patient.* **(Ma et al., 2010)**

Virtual reality (VR) using immersion and interaction may provide new approaches to the treatment of ***memory deficits*** *in* ***elderly*** *individuals.* **(Optale, 2010)**

c) **as suas características: imersiva, interativa, realista, de feedback, tempo real, controlo de estímulos complexos, entre outras**

The value of the technology of virtual environments in this context is that it allows us to ***immerse*** *people with brain damage in relatively* ***realistic interactive*** *environments which (…)* **(Rose et al, 1997)**

Virtual environments (VE's) let users navigate and ***interact*** *with computer-generated* ***three-dimensional (3-D)*** *environments in* ***real time****, allowing for the* ***control of complex stimuli*** *presentation.* **(Riva et al., 1998)**

Due, in large part, to the significant advances in PC hardware that have been made over the last 3 years, PC-based virtual environments are ***approaching reality****.* **(Riva et al., 1999)**

And Virtual Reality technology can hold a patient's attention for a longer period of time than other methods can, because VR is ***immersive, interactive and imaginal****.* **(Cho et al., 2002)**

Enhanced feedback *provided by a virtual reality system has been shown to promote motor learning in normal subjects.* **(Piron et al., 2005)**

It can provide a ***safe setting*** *in which to practice skills that might carry too many risks in the real world. Unlike human tutors, computers are* ***infinitely patient and consistent****. (…) Virtual worlds can be* ***manipulated*** *in ways the real world cannot be and can* ***convey concepts without the use of language or other symbol systems****.* **(Standen et al., 2005)**

Virtual Reality (VR) with ***multimodal displays has the chance to feed back performance information*** *to the patient, augment the* ***training*** *with additional* ***audiovisual features****, thus, making the therapy more* ***exciting*** *and increasing patient motivation.* **(Riener et al, 2006)**

Virtual reality offers the option to produce and distribute identical ***"standard" simulation*** *environments in which performance can be measured and rehabilitated.* **(Rizzo et al., 2006)**

Virtual reality (VR) provides a unique environment where the ***presentation of stimuli can be systematically controlled to enable an optimal level of challenge by progressing task difficulty as performance improves****.* **(Stewart et al., 2006)**

Virtual reality (VR)-based techniques have the potential to solve these difficulties, because they provide a computer-generated but ***realistic three-dimensional world*** *and* ***humanlike avatars that can provide emotional stimuli****.* **(Ku et al., 2007)**

Virtual reality systems have been used to deliver ***goal directed repetitive training*** *to promote rehabilitation of individuals post-stroke.* **(Mirelman et al., 2007)**

For the second case, a neurofeedback (NFB) system was established, which utilized Virtual Reality (VR) to create ***appropriate feedback information which is more interesting, imaginative and interactive*** *than traditional graphical presentations.* **(Wang et al., 2007)**

Those results will support the use of virtual reality for situated neglect assessment and provide guidelines for rehabilitation trials in ***more ecologically-like contexts****.* **(Morganti et al., 2007)**

Virtual reality (VR) facilitates learning in a ***safe environment*** *enabling a* ***gradual increase in the complexity of tasks*** *approaching the* ***conditions of real life****.* **(Josman et al., 2008)**

Our VR-based intervention addresses this issue, by providing a ***high ecological validity therapeutic tool****.* **(Anton et al., 2009)**

d) consequências das características

*The value of the technology of virtual environments in this context is that it **allows us to immerse people with brain damage in relatively realistic interactive environments which**, because of their patterns of impairment, **would otherwise be unavailable to them**.* **(Rose et al, 1997)**
*Within such digital scenarios, **normative data can be accumulated for performance comparisons** needed for assessment/diagnosis and for treatment/rehabilitation purposes.* **(Rizzo et al., 2006)**
*Moreover, the use of VR-based scenarios in which patients perform rehabilitation exercises **dramatically increases the patients' motivation and thus the final therapy outcome**.* **(Montagner et al. 2007)**
*It induces **brain plasticity** and benefits may be **transferable to the physical world**.* **(Guberek et al., 2008)**
*Virtual reality (VR) constitutes a promising alternative of approximation to real life that may help increase the level of **generalization of skills developed** in programs that use this kind of technology*. **(Dores et al., 2009)**

e) superar limitações dos testes/intervenções tradicionais

*It is suggested that virtual reality can be used in MS patients to assess aspects of spatial memory that **are not measured by traditional tests.*** **(Pugnetti et al., 1998)**
*And Virtual Reality technology can hold a patient's attention for a longer period of time **than other methods can**, because VR is immersive, interactive and imaginal.* **(Cho et al., 2002)**
*Virtual reality (VR) has the potential to **assist current rehabilitation techniques** in addressing the impairments, disabilities, and handicaps associated with brain damage.* **(Rose et al. 2005)**
*Virtual reality-based evaluation will also provide evidences of neglect induced biases in coping with everyday contexts that **could be unclear detectable in paper and pencil assessment**.* **(Morganti et al., 2007)**

Limitações da RV surgiram relacionadas com:

a) os efeitos secundários

*Although there is much potential for the use of immersive virtual reality environments in clinical applications, there are problems which could limit their ultimate usability. Some users have experienced **side-effects during and after exposure to virtual reality environments.** The symptoms include **ocular problems, disorientation and balance disturbances, and nausea.*** **(Lewis et al., 1997)**
*Issues addressed in this project include: the occurrence of VE-related **side effects** in healthy older adults* **(McGee et al., 2000)**
*For expanding application of virtual reality, such as rehabilitation engineering, concerns of **<u>cybersicknes</u>** should be cleared.* **(Kiryu et al., 2005)**

b) as causas das limitações

*Susceptibility to side-effects can be affected by **age, ethnicity, experience, gender and physical fitness, as well as the characteristics of the display, the virtual environment and the tasks. The characteristics of the virtual reality system have also been shown to affect the ability of users to perform tasks in a virtual environment. Many of these effects can be attributed to delays between the sampling of head and limb positions and the presentation of an appropriate image on the display.*** **(Lewis et al., 1997)**
*Although virtual simulation offers a range of new possibilities, **learning to navigate in a virtual environment is not equivalent to learning to navigate in the real world**.* **(Cooper et al. 2005)**
*(...) has been successfully applied in various fields such as engineering, medicine, training, and high-quality 3D games, **but few VR therapy systems currently support physics**.***(Ma et al., 2006**)
*However, there are **some concerns over whether people with ASDs can understand, use and interpret the technology appropriately**.* **(Parsons et al., 2006**)
*Many tasks have been developed in VEs, but **few have shown effective transfer of training**.*

(Pridmore et al., 2007)
However, there is ***little evidence of the effectiveness of training in a virtual environment (VIE) compared to training in a real-world physical environment (PE) regarding the improvement in upper limb impairment and functional levels post-stroke.*** **(Subramanian et al., 2007)**
The adoption of Virtual Reality in rehabilitation of cognitive and psychological disorders is limited by ***high costs of software*** *development,* ***lack of technical expertise*** *among end-users, and the* ***difficulty of adapting the contents*** *of the virtual environments (VEs).* **(Riva et al., 2007)**
People with brain injury may be ***less tolerant to a poor interface and a VE might therefore become unusable due to, for example, an unsuitable input device. (Wallergard et al., 2007)***
It is concluded that difficulties in ***adapting programs to specific clinical needs****,* ***technical issues, and the reluctance of many clinicians*** *to use computer-based technology need to be overcome before VR is likely to be widely used to measure PM.* **(Knight et al., 2009)**
A limiting factor in the innovation and the acceptance of virtual environments with haptic feedback is the ***time and cost*** *required to build them, (****Zhu et al., 2009)***
(…) we can establish that ***it is not sufficient the acquisition and use of high technology in the assessment/treatment of patients with disabilities****.* **(Villanueva et al., 2009)**
Results show differences in ***VR spatial brain processing as compared to known brain activations in reality.*** *Identifying differences and commonalities of brain processing in VR reveals limitations and holds important implications for VR therapy and training tools. (…) When VR therapy aims at the rehabilitation of brain function and activity, differences in brain processing have to be taken into account for designing effective VR training tools.* **(Beck et al., 2010)**
Published ***clinical studies evaluating its acceptance, potential benefits and side-effects*** *in the rehabilitation of patients with post-stroke weakness* ***are few*** *in number.* **(Joo et al., 2010)**
The type of virtual objects used for reaching tasks varies widely, but there has been ***little work exploring the effect of different characteristics of objects on target acquisition time.*** **(Powell et al., 2010)**
Although existing evidence suggests that increasing intensity of stroke rehabilitation therapy results in better motor recovery, ***limited evidence is available on the efficacy of virtual reality for stroke rehabilitation.*** **(Saposnik et al., 2010)**
However, the ***current level of evidence is poor*** *and* ***empirical data is lacking****.* ***Future methodologically rigorous studies are required.*** **(Snider et al., 2010)**

c) **precauções**

Special precautions therefore need to be taken to ensure the safety and effectiveness of such virtual reality applications. These precautions include minimisation of possible side-effects at the design stage. *Factors are identified which are likely to affect the incidence of side-effects during and after exposures, and* ***which need to be understood in order to minimise undesirable consequences.*** *There is also a need for the* ***establishment of protocols for monitoring and controlling exposures*** *of patients to virtual reality environments. Issues are identified which need to be included in such protocols.* **(Lewis et al., 1997)**
However, ***basic feasibility issues need to be addressed*** *for this technology to be reasonably and efficiently applied to the cognitive rehabilitation (CR) of persons with acquired brain injury and neurological disorders.* ***(****Rizzo, Buckwalter, & Neumann, 1997)**
(…) we can establish that ***it is not sufficient the acquisition and use of high technology in the assessment/treatment of patients with disabilities****, but* ***it is necessary to know the scope and limitations of each system, learn to using the technology, covering the period of the learning curve and become the data from this technology in useful information for clinical application****.* **(Villanueva et al., 2009)**

DISCUSSÃO

O crescente número de publicações nesta área (Figura 1) evidencia o interesse atual pela RV e a sua pertinência como área de investigação. Da literatura revista resultou um melhor recorte conceptual acerca desta tecnologia e do seu contributo em diversos domínios, bem como um conhecimento mais pormenorizado das suas principais limitações. Entre elas, a necessidade de: (1) superar dificuldades associadas aos custos e tempo de desenvolvimento; (2) conhecer os fatores que contribuem para os efeitos secundários e minimizá-los; (3) adaptar ou desenhar ambientes que considerem as especificidades das patologias; (4) melhorar a metodologia dos estudos de análise dos impactos. No que concerne aos aspetos metodológicos, revelam-se necessários: (1) estudos com amostras maiores; (2) a introdução de grupo de controlo; (3) maior uniformização nos testes aplicados na avaliação de determinadas variáveis; e, ainda, (4) estudos de *follow-up*. Estas dimensões facilitarão a comparação interestudos e a generalização de resultados, permitindo dados com maior validade e fidelidade acerca da utilização da RV numa diversidade de quadros de diagnóstico. No lado das vantagens, é de salientar: (1) a possibilidade de aplicação a uma diversidade de domínios, de funções cognitivas, comportamentos, doenças neurológicas e incapacidades físicas, (2) as características inovadoras da RV que permite ultrapassar limitações das intervenções tradicionais. É ainda reconhecido o enorme potencial desta tecnologia, assistindo-se a um esforço crescente de validar a sua utilização na reabilitação em geral e em particular na reabilitação (neuro)cognitiva.

É de ressalvar a existência prévia de estudos de revisão da literatura acerca das aplicações da RV[18, 35]. Contudo, esses estudos exploram apenas áreas específicas da sua aplicação. Neste trabalho, a metodologia estrutural utilizada é nova nesta área e além de atual, considera a aplicação da RV à reabilitação de um modo global. Caracterizar esta realidade, nas suas vantagens e limitações, foi o principal objetivo deste trabalho, que procurou dar resposta acerca da utilização da RV àqueles que exercem clínica ou investigam neste domínio, através de informação mais sistematizada.

CONCLUSÕES

Em resposta à questão por nós colocada, este estudo evidencia mais trabalhos e razões para a utilização da RV do que o contrário. O facto de serem identificadas limitações da RV, passado o entusiasmo excessivo veiculado pelos *media*, e de diversos autores e grupos de investigação procurarem ultrapassar tais limitações, reforça ainda mais a vantagem da utilização desta tecnologia na reabilitação em diversos domínios, bem como a importância da investigação continuada nesta área, no sentido de melhorar a aplicação desta ferramenta.

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Artigo 2 - Conceptualizations and Rehabilitation in Executive Functions: A Systematic Literature Review.

Dores, A. R., Carvalho, I. P., Barbosa, F., Martins, C., de Sousa, L., & Castro-Caldas, A. (submetido). Conceptualizations and rehabilitation in executive functions: A systematic literature review.

Conceptualizations and rehabilitation in executive functions: A systematic literature review

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Abstract

Publications on executive functions (EF) have increased in the last few years, which reflect the importance of this area of study. The scientific production on EF is now extremely diverse, comprehending variations around terminology, assessment and rehabilitation practices, and ranging in topics from neuroanatomical correlates of EF to effects of executive dysfunction.

This review seeks to explore this diversity around EF in order to provide an integrative overview of this topic that systematizes the current knowledge in this area, and to point to trends and future directions for research and practice.

The literature review was conducted on scientific papers indexed, until April 2011, in the ISI Web of Knowledge databases. The analysis was conducted in NVivo9. Two independent coders applied an inductive analysis to all relevant papers, building a hierarchical model with categories and sub-categories of themes emerging from the literature. A confirmatory analysis followed, with the same independent coders applying the model to the papers. The process was validated by a third, expert researcher.

Out of 187 titles and abstracts, 91 were analyzed. The outcomes were structured in eight main categories, two pertaining to ‘Article Type’ and ‘Scientific Domain’, and six referring to emerging themes: ‘Central Nervous System, Diagnosis, Population, Assessment, Intervention, and Theoretical Models’.

Key findings included promising trends in assessment and rehabilitation, and potential implications for current health approaches and for future research.

Keywords: Executive functions; Acquired brain injury; Systematic literature review.

Introduction[7]

The number of publications on executive functions (EF) has increased in the last few years, which reflects the importance and complexity of this area of study. New tools that could optimize research and intervention on these functions have also emerged. The scientific production on EF is now extremely diverse, comprehending many variations around terminology, assessment and rehabilitation practices, and ranging in topics from neuroanatomical correlates of EF to effects of executive dysfunction.

Lezak coined the term 'executive function', presenting it as involving skills to formulate goals, to plan strategies to achieve those goals, and to self-evaluate one's performance during these activities (Lezak, 1982, 1987). She conceptualized EF in four components or sub-processes: volition, planning, purposive action, and effective performance (Lezak, Howieson, & Loring, 2004). Since then, hundreds of authors have focused on the study and conceptualization of this construct (Fuster, 1997; Pennington, 1997; Roberts & Pennington, 1996; Stuss & Benson, 1984, 1986). However, the construct and its definition are still complex and unclear, which is reflected, for example, in the diversity of terms that can be found in the literature to designate executive functioning.

Despite the wide range of views about this functioning, there is increasing consensus about the fact that EF are not a unitary construct (Robbins, 1996). This assumption gathers support from clinical, pathophysiological, and functional neuroimage evidence (Masterman & Cummings, 1997), though a central executive, that could be the executive attention system or working memory, has been recently suggested to provide some unity to EF (McCabe, Roediger III, McDaniel, Balota, & Hambrick, 2010).

Considering the nature and diversity of EF sub-processes, there are various difficulties associated with their assessment and rehabilitation. One such difficulty has to do with the ecologic validity of the instruments used to measure EF - traditionally neuropsychological tests. The artificial situation in which these tests are performed, compared with real life, has been criticized. The instruments to be used and the proposal of alternative methods of assessment are frequently addressed in the literature.

EF rehabilitation is another major concern. When EF are damaged, becoming disrupted, other mental functions that were preserved before also tend to become affected, producing general cognitive and behavioral disorganization. Executive dysfunction, or dysexecutive syndrome, can be rather pervasive and disabling to patients and their families (Baddeley, 1986; Baddeley & Wilson, 1988). In these cases, neuropsychological rehabilitation aims at 'shifting the individual from a more dependent, externally supported state to a more independent and self-regulated state' (Mateer, 1999,

[7] As referências bibliográficas deste artigo encontram-se no formato proposto pela revista a que foi submetido.

p. 50). Accordingly, the biggest and most important goal of rehabilitation is to improve the patient's functioning in daily life and to ensure better quality of life and functionality, as much as possible. This implies not only the transfer, but also the generalization of the acquired abilities to real life – a goal that literature has addressed.

The role and functioning of the prefrontal cortex have been central to the understanding of EF, since this structure is concerned with the regulation of mental activities (Bechara, Damasio, & Damasio, 2000; Luria, 1973, 1980). The prefrontal cortex is regarded as a heteromodal association area, connected with cortical and subcortical regions (Tirapu-Ustarroz, Garcia-Molina, Luna-Lario, Roig-Rovira, & Pelegrin-Valero, 2008a), and in which specific contributions are attributed to different functional circuits. For example, the dorsolateral section is more involved in purely cognitive activities, such as those having to do with working memory or selective attention, whereas the ventromedial section is associated with the processing of emotional signals that are relevant to decision making processes. A variety of theories or models have offered different conceptualizations of the role of prefrontal regions in EF, provided functional explanations for the processes underlying these functions and/or facilitated the study of the complex relationship between EF and behavior. In two recent works, Tirapu-Ustarroz, Garcia-Molina, Luna-Lario, Roig-Rovira and Pelegrin-Valero (2008a; 2008b) presented a review of the main existing theoretical models (e.g., Hierarchical model, Working memory and executive functions model, Hypervigilant attentional system, Somatic marker model, Integrative model, Dynamic filter theory, Theory of cognitive complexity and control, Model of differential axis in the executive control, Hypothesis of the frontal lobes' hierarchical representation, Supervisor attentional system, Model of attentional control, Rostrolateral prefrontal cortex model and Christoff and Burgess's models). This review demonstrates the complexity of EF and the efforts to understand their nature. These efforts are also reflected in the growing theoretical and empirical literature in this area.

Given the current diversity around EF in scientific literature, this review seeks to explore this diversity and to provide an integrative overview of this topic that systematizes the current knowledge in terms of the themes that emerge from the literature.

Material and methods

General stages and protocols of this study's design follow suggestions by Tranfield and colleagues (2003) and Creswell (2003). A systematic literature review of scientific papers indexed in the ISI Web of Knowledge databases until April 26, 2011, was conducted. Keywords and search string were: (executive dysfunction* OR dysexecutive function* OR dysexecutive syndrome OR executive function*) AND ('traumatic brain injury'

OR TBI OR ‘acquired brain injury’ OR ABI OR ‘neurologic* diseases’ OR ‘neurologic* disorders’) AND (model* OR review). The choice of search string terms was derived from the literature in the field.

A total of 187 abstracts were found between 1994 and 2011. Excluding criteria were: (1) topics outside of the scope of this study’s goal, such as immunology, endocrinology and metabolism, ethnic studies, legal medicine, information science and library science, obstetrics and gynecology, ophthalmology, reproductive biology, demography, mathematics, among others; (2) ‘Languages’ other than English; and (3) documents from meetings. After the application of the excluding criteria, 91 records were retained for analysis.

These articles (Appendix 1) were exported to an Endnote library and their titles and abstracts were then exported to NVivo 9 (2011, QSR, Victoria). The analysis was conducted on the 91 papers’ titles and abstracts by two independent reviewers and validated by a third one – expert researcher.

A first and general analysis of the themes and terminology in the literature explored the most frequent words in all abstracts and titles. Then the analysis proceeded in two phases. First an inductive analysis (without previous categories) was conducted to identify key concepts. Two reviewers built a hierarchical tree of their respective codes. Similar codes of the two reviewers were merged, and a preliminary model was built describing the nature and quality of the information. Then, findings were obtained comparing the analysis of the two reviewers and reaching consensus, with a final validation by the third, independent expert researcher. The final model was then constructed.

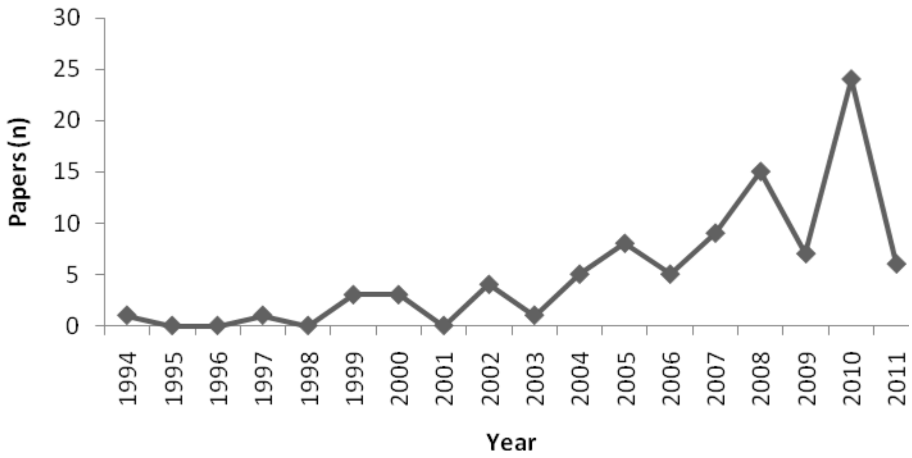
In order to validate the original coding, the two reviewers used the developed framework and applied it to re-code all the material. The re-coding was conducted independently. The goal was to test the robustness and external validity of the previously developed framework. It also allowed to check the internal validity and to reach an agreement over both construct and concept validity of the hierarchical tree.

Inter-rater level of agreement, which is generally considered a more robust measure than simple percent agreement calculation, since it takes into account agreement occurring by chance, was 0.86 for *Cohen's kappa* coefficient. The agreement between the two reviewers (mean of agreement in all categories) was of 96.71 (*SD*=10.35). Final data were analyzed through descriptive statistics.

Results

Scientific production

Figure 1 shows that the number of publications on EF has been increasing over the past years, peaking in 2010 (n=23; 25.27%), which indicates the current interest in the topic. The three journals with more publications in this domain were 'Neuropsychological Rehabilitation' (n=12; 13.19%); 'Brain Injury' (n=7; 7.69%) and 'Journal of Head Trauma Rehabilitation' (n=6; 6.59%). The authors with more publications were Gioia, Cicerone, Chevignard, Feeney and Ownsworth, with two papers each.



Most frequent words

Table 1 shows the 20 most frequent words in the analyzed documents (words appearing more than 50 times in all works reviewed), after exclusion of irrelevant words, such as "were", "more", "self", "from," and of words with a length of less than three characters.

Table 1 - Most frequent words

Word	Word count (n)	Word weighted percentage (%)
Executive	213	6.66
Brain	179	5.60
Injury	164	5.13
Cognitive	163	5.10
TBI	129	4.04
Traumatic	99	3.10
Rehabilitation	82	2.56
Review	78	2.44

Function	75	2.35
Memory	75	2.35
Children	73	2.28
Functioning	68	2.13
After	66	2.06
Social	66	2.06
Patients	65	2.03
Model	60	1.88
Assessment	59	1.85
Deficits	59	1.85
Functions	57	1.78
Studies	50	1.56

Word count = number of times the words appeared.

Word weighted percentage = % of each word in the total of words.

Main themes (NVivo model)

Papers varied in terms of ‘Article Types’ (n=91 records; 100% of all) and of ‘Scientific Domain’ (n=91 records; 100% of all) (Table 2). The main themes emerging from the literature were, in descending order, ‘Central Nervous System’ (n=86 records; 95% of all), ‘Diagnosis’ (n=82 records; 90% of all), ‘Population’ (n=72 records; 79% of all), ‘Assessment’ (n=61 records; 67% of all), ‘Intervention’ (n=54 records; 59% of all) and ‘Theoretical Models’ (n=41 records; 45% of all).

Table 2 - Paper variation in terms of ‘Article Types’ and ‘Scientific Domain’

	No of records	% in the (sub)category	% of all
Review	91	100	100
Article Types	91	100	100
Literature Review	51	56	56
Empirical articles	40	44	44
Scientifc Domain	91	100	100
Neuropsychology	82	90	90
Neurosciences	25	27	27
Social Sciences	9	10	10
Neuropsychiatry	2	2	2
Psychology	1	1	1

Other	1	1	1

1. *Article Types:* Fifty-one records are 'Literature review' articles (56%) and 40 are 'Empirical' articles (44%).
2. *Scientific Domain:* Eighty-two articles fall within the area of 'Neuropsychology' (90%), 25 of 'Neurosciences' (27%), nine of 'Social Sciences' (10%), two of 'Neuropsychiatry' (2%), one of 'Psychology' (1%), and one refers to 'Other' areas (1%).

Of the emerging themes, '*Diagnosis', 'Population'* and '*Theoretical Models'* all had a one-layered sub-division (Table 3):

Table 3 - Paper variation in terms of 'Diagnosis', 'Population' and 'Theoretical Models'

	No of records	**% in the (sub)category**	**% of all**
Diagnosis	82	90	90
Types	82	100	90
Consequences	72	88	79
Population	72	79	79
Children	26	36	29
Adolescents & Youths	15	21	16
Adults	13	18	14
Older Adults	4	6	4
Animals	4	6	4
Population Country	2	3	2
Unspecified	33	46	36
Theoretical Models	41	45	45
Neuropsychological	30	73	33
Social	7	17	8
Assessment	6	15	7
TBI	6	15	7
Rehabilitation	5	12	5
Awareness	4	10	4
Memory	4	10	4
Attention	3	7	3

Animals	1	2	1
Autism Spectrum D.	1	2	1

3. *Diagnosis:* Eighty two articles report ‘Types’ of diagnosis (90%) and 72 report ‘Consequences’ of the diagnoses (79%). Example of ‘Types’ of Diagnosis:

Impairment in executive functioning can occur after mild stroke, mild Traumatic Brain Injury, and neurodegenerative disease (…) (Dodson, 2010).

4. Population: Twenty six articles report on ‘Children’ (29%), 15 on ‘Adolescents and Youths’ (16%), 13 on ‘Adults’ (14%), four report on ‘Older Adults’ (4%), four on ‘Animals’ (4%), two on ‘Population Country’ (2%), and 33 did not specify the studied population (36%). Example of references to ‘Children’:

Construct and criterion validity of the Behaviour Rating Inventory of Executive Function (BRIEF) in children referred for neuropsychological assessment after paediatric traumatic brain injury (Donders, DenBraber, & Vos, 2010).

5. *Theoretical Models:* Thirty articles report on ‘Neuropsychological’ models (33%), seven on ‘Social’ models (8%), six on ’Assessment’ models (7%), six on ‘TBI’ models (7%), five on ‘Rehabilitation’ models (5%), four on ‘Awareness’ models (4%), four on ‘Memory’ models (4%), three on ‘Attention’ models (3%), one on ‘Animal’ models (1%) and one on ‘Autism Spectrum Disorder’ models (1%). Example of ‘Neuropsychological’ models:

The models put forward to date approach the same reality from a number of different perspectives in some case avoiding certain parts of that reality. In this first part, we review the models and theories of contextual information, structured complex events, working memory, adaptive encoding, Miller and Cohen's integrating theory, and the factorial models of executive control (Tirapu-Ustarroz, et al., 2008a).

The themes ‘Central Nervous System’, ‘Assessment’ and ‘Intervention’ were subdivided in several child nodes (Table 4):

Table 4 - Paper variation in terms of ‘Central Nervous System’, ‘Assessment’ and ‘Intervention’

	No of records	**% in the (sub)category**	**% of all**
Central Nervous System	86	95	95
(Dys)Functions	85	99	93
Cognitive (Dys)Functions	83	98	91
Executive Function	72	87	79

			Terminology	68	94	75
			Components	32	44	35
		Memory		36	43	40
		Attention		31	37	34
		Language		14	17	15
		Information Processing		12	14	13
		Learning		11	13	12
		Problem Solving		9	11	10
		Intelligence Quotient		6	7	7
		(Un)Awareness		5	6	5
		Perception		4	5	4
		Visuospatial Functioning		1	1	1
		Unspecified		22	27	24
	Behavioral Functioning			23	27	25
	Social Skills			20	24	22
	Physical (Dys)Functions			11	13	12
	Other			47	55	52
Structures				33	38	36
Lesions				27	31	30
	Types			26	96	29
	Consequences			20	74	22
Assessment				61	67	67
Types				58	95	64
	Neuropsychological			46	79	51
	Neurological			15	26	16
	Physical			10	17	11
	Behavioral			5	9	5
	Other			8	14	9

	Instruments		46	75	51
		Psychometric	26	57	29
		Neuroimage	12	26	13
		Other	10	22	11
		Unspecified	6	13	7
	Recommendations		16	26	18
	Limitations		13	21	14
	Validity		10	16	11
	Professionals		5	8	5
Intervention			54	59	59
	Types		49	91	54
		Cognitive Rehabilitation	32	65	35
		Cognitive-Behavioral	8	16	9
		Social	6	12	7
		Pharmacological	6	12	7
		Psychological	3	6	3
		Physical	2	4	2
		Psychotherapy	1	2	1
		Unspecified	19	39	21
	Strategies		33	61	36
	Recommendations		32	59	35
	Limitations		14	26	15
	Professionals		6	11	7
	Instruments		3	6	3

6. *Central Nervous System:* Eighty five articles report ‘(Dys)functions’ (93%), 33 refer ‘Structures’ involved (36%) and 27 report ‘Lesions’ (30%).
   6.1. As part of (Dys)Functions, 83 articles report ‘Cognitive (Dys)Functions’ (91%), 23 report ‘Behavioral Functioning’ (25%), 20 report ‘Social Skills’ (22%), 11 report ‘Physical (Dys)Functions’ (12%), and 47 refer to other (Dys)Functions (52%).
   6.1.1. As part of ‘Cognitive (Dys)Functions’, 72 articles (79%) refer to ‘Executive Functions’, 36 to ‘Memory’ (40%), 31 to ‘Attention’ (34%), 14 to Language (15%), 12 to ‘Information Processing’ (13%), 11 to ‘Learning’ (12%), nine to ‘Problem

Solving' (10%), six to 'Intelligence Quotient' (7%), five to '(Un)Awareness' (5%), four to 'Perception' (4%), one to 'Visuospatial Functioning' (1%), and 22 (24%) are Unspecified.

6.1.1.1. As part of 'Executive Functions', 68 articles report 'Terminology' (75%) and 32 report executive function 'Components' (35%). Example of 'Terminology':

The cognitive skills that allow individuals to control and regulate their behaviour are called executive functions (Tirapu-Ustarroz, et al., 2008a). Example of 'Components':

EF include inhibition of behavior and irrelevant information, nonverbal working memory, verbal working memory, self-regulation of affect, motivation and arousal, planning, decision making, self monitoring of the entire solving problem process and self evaluation of the results of the action taken (Papazian, Alfonso, & Luzondo, 2006).

6.2. 'Structures' was not subdivided. The recognized neural substrate of EF is the (pre)cortex. However, recent articles emphasize the importance of frontal-cortical-subcortical circuits, i.e., the importance of active and flexible networks and the mediation of dopaminergic neurotransmitters. Example of Structures:

Damage to the frontal structures may lead to a diverse set of changes in cognitive, behavioral, or emotional domains. While lesion studies have demonstrated distinct impairments related to pathology in different frontal regions, it is clear that the frontal lobe syndrome is not restricted to damage to frontal regions. (…) *Since no one specific neurologic disorder has a predilection to damage isolated to the frontal lobes, profiles of the dysexecutive syndrome are related to damage to several regions in addition to the frontal lobes* (Hanna-Pladdy, 2007).

6.3. As part of 'Lesions', 26 papers report 'Types' of lesions (29%) and 20 refer 'Consequences' of lesions (22%). Example of 'Types' of lesions:

In this study, the effectiveness of a group-based attention and problem solving (APS) treatment approach to executive impairments in patients with frontal lobe lesions was investigated (Miotto, Evans, de Lucia, & Scaff, 2009).

7. *Assessment:* Fifty eight articles report on 'Types' of assessment (64%), 46 on 'Instruments' used (51%), 16 on 'Recommendations' for assessment (18%), 13 on assessment 'Limitations' (14%), ten on assessment 'Validity' (11%), and five on 'Professionals' involved (5%).

7.1. As part of assessment 'Types', 46 articles report on 'Neuropsychological' assessment (51%), 15 on 'Neurological' assessment (16%), 10 on 'Physical' assessment (11%), five on ‘Behavioral’ assessment (5%), and eight on ‘Other’ assessment types (9%). Example of ‘Neuropsychological’ assessment type:

Executive clock drawing correlates with performance-based functional status in people with combat-related mild traumatic brain injury and comorbid posttraumatic stress disorder (Writer, Schillerstrom, Regwan, & Harlan, 2010).

7.2. As part of the ‘Instruments’, 26 articles report on ‘Psychometric’ instruments (29%), 12 on ‘Screening’ instruments (13%), ten on ‘Other’ instrument types (11%), and six did not specify the instruments (7%). Example of ‘Psychometric’ instruments:

In this study we explore the dimensional structure of a tool designed to assess level of executive functioning, the Dysexecutive (DEX) Questionnaire (Burgess, Alderman, Wilson, Evans, Emslie, 1996), in order to inform theoretical conceptualisations of executive functioning and improve measurement precision in rehabilitation centres (Simblett & Bateman, 2011).

7.3. ‘Recommendations’, ‘Limitations’, ‘Validity’, and ‘Professionals’ were not subdivided. Examples of ‘Recommendations’:

Guided by the International Classification of Functioning, Disability, and Health model (ICF model; Peterson, 2005), we suggest that an important development in the field is moving to formal assessment of executive performance in functional contexts, in addition to more traditional assessment of executive impairment (Lewis, Babbage, & Leathem, 2011).

As we take what we learned from Mark Ylvisaker, it becomes increasingly apparent that our assessment and intervention methods, especially as related to the executive functions, demand an everyday, real-world context (Gioia, Kenworthy, & Isquith, 2010).

Examples of ‘Limitations’:

We discuss the obstacles to accurate measurement of executive control, such as: its prolonged developmental trajectory; lack of consensus on its definition and whether it is a unitary construct; the inherent complexity of executive control; and the difficulty measuring executive-control functions in laboratory or clinical settings (Kenworthy, Yerys, Anthony, & Wallace, 2008).

Working memory is the most severe type of executive dysfunction and may not be adequately measured by current neuropsychological evaluation methods (Matheson, 2010).

D*espite these high proportions and detrimental effects, few studies have utilized a developmentally appropriate, standardized measure to assess executive functioning within a pediatric TBI population* (Johnson-Bauman, Maricle, Miller, Allen, & Mayfield, 2010).

The study proposes the use of alternate, equivalent tasks to help eliminate the effects of practice associated with serial assessment (Atkinson & Ryan, 2008).

Example of 'Validity':

The construct and criterion validities of the parent version of the Behaviour Rating Inventory of Executive Function (BRIEF) were evaluated in a sample of 100 6- to 16-year-old children with traumatic brain injury (TBI) (Donders, et al., 2010).

Examples of 'Professionals':

Clinical neuropsychologists have adopted numerous (and sometimes conflicting) approaches to the assessment of brain-behavior relationships (Stuss & Levine, 2002).

Clinicians are often asked to make an assessment on whether a patient is medically fit to drive, even though few have been formally trained in this area (Yale, Hansotia, Knapp, & Ehrfurth, 2003).

8. *Intervention:* Forty nine articles report on 'Types' of interventions (54%), 33 on intervention 'Strategies' (36%), 32 on 'Recommendations' (35%), 14 on Intervention 'Limitations' (15%), six on 'Professionals' involved (7%) and three on 'Instruments Used' for intervention (3%).

8.1. As part of intervention 'Types', 32 articles report 'Cognitive Rehabilitation' (35%), eight 'Cognitive-Behavioral' intervention (9%), six 'Social' intervention (7%), six 'Pharmacological' intervention (7%), three 'Psychological' intervention (3%), two articles report 'Physical' intervention (2%), one refers 'Psychotherapy' (1%) and 19 refer 'Unspecified' interventions (21%). Examples of 'Cognitive Rehabilitation':

Assessing executive performance during cognitive rehabilitation (…). Therefore, assessment of a person's executive functioning is a high priority as part of a comprehensive neurorehabilitation plan (Lewis, Babbage, & Leathem, 2011).

8.2. 'Strategies', 'Recommendations', 'Limitations', 'Professionals' and 'Instruments' were not subdivided. Examples of 'Strategies' to be used in intervention:

Examples of 'Strategies':

Improving the patient's functioning in the real-world environment must be the major goal, and as such intervention methods require an everyday, real-world contextualization (Gioia, et al., 2010).

Motivational Interviewing to promote self-awareness and engagement in rehabilitation following acquired brain injury: A conceptual review (Medley & Powell, 2010).

Examples of 'Recommendations':

The review of available evidence points to four major recommendations for the rehabilitation of cognition following brain injury: 1) Access to subacute rehabilitation that is holistic in nature and involves a multidisciplinary or transdisciplinary team to work in an integrated fashion to support physical, cognitive, and social skill retraining is vital to support positive outcome following TBI. (…) 2) Trials of medication, especially methylphenidate, to assist individuals with significant attention and memory impairment appear well supported by the available evidence. 3) Randomized controlled trials demonstrate the utility of specific rehabilitation approaches to attention retraining and retraining of executive functioning skills. Future research is needed on rehabilitation techniques in other domains of cognition. 4) Training in the use of supportive devices (either a memory book or more technologically enhanced compensatory devices) to support the individual's daily activities remains central to the independent function of the individual in the community. Though emerging treatments (eg, virtual reality environments) show relative degrees of promise for inclusion in the rehabilitation of the individual with TBI, these need further evaluation in systematic trials (Cernich, Kurtz, Mordecai, & Ryan, 2010).

Examples of ‘Limitations’:

Additionally, treatments for cognitive impairments after HI-BI are underdeveloped and are generally arrived at by analogy to the treatment of such problems arising from other neurological conditions, especially traumatic brain injury (Anderson & Arciniegas, 2010).

The benefits of rehabilitation following acquired brain injury (ABI) are all too often disrupted by a lack of engagement in the process, variously attributed to cognitive, emotional and neurobehavioural sequelae, and prominently to impaired self-awareness of deficits (Medley & Powell, 2010).

Examples of ‘Professionals’:

While individual disciplines are not directly referred to in this paper, input from a comprehensive and co-ordinated interdisciplinary team is crucial to understanding and reducing the impact of executive deficits on functional performance (Galvin & Mandalis, 2009).

Examples of ‘Instruments’:

The evidence base for the rehabilitation of PM is then considered, focusing on retraining PM, using retrospective memory strategies, problem-solving training, and finally, electronic memory aids (Fish, Wilson, & Manly, 2010).

Discussion

Most frequent words

The analysis of the *most frequent words* allows a first understanding of the themes considered in the articles. Those that emerge in this first analysis have to do with how this construct is named (e.g., executive function, EF, executive functioning), what the etiology of executive dysfunction is (e.g., Brain Injury, Traumatic Brain Injury or TBI) and which brain structures are involved, what the consequences are (e.g., social deficits), assessment and rehabilitation issues, other cognitive functions involved (e.g., memory), and population affected (e.g., children). They also refer to the type of article considered (e.g., review, studies), to theoretical models, and to brain correlates. Several of these words were expected, since they were included in the search equation. Most of these themes appear in the subsequent analysis, represented in the developed NVivo model.

Themes identified in the literature (NVivo model)

In what concerns ‘Article Types’, most of the papers are literature reviews. Because theoretical papers can provide particularly good insights into trends and approaches to a topic of study, they are seminal to the purposes of this work. Accordingly, ‘review’ was one of the keywords in the search string, possibly having directed the search to this particular type of articles.

Indicating the nature of the works reviewed, the vast majority of themes appeared under the ‘Scientific Domain’ of ‘Neuropsychology’ (specifically, emphasizing the relation between brain, and cognitive, emotional and behavioral systems) and ‘Neurosciences’ (the scientific study of the nervous system). The intersection of neuroscience and cognitive psychology also is reflected, for example, in the combined use of different research methodologies, including hemodynamic approaches (e.g., fMRI), that allow the assessment of how brain regulations may relate to behavioral and cognitive measures.

Different ‘Types’ of ‘Diagnoses’ appear associated with deficits in specific cognitive functions. Those more closely related with executive dysfunctions are mainly Traumatic Brain Injury (TBI) (e.g., Cicerone, et al., 2011) with or without comorbid Posttraumatic Stress Disorder (PTSD) and Acquired Brain Injury (ABI) (e.g., Simblett & Bateman, 2011). Other diagnoses associated with cognitive deficits are Autism Spectrum Disorders (ASD) (e.g., Schroeder, Desrocher, Bebko, & Cappadocia, 2010; Serruya & Kahana, 2008), cancer, cerebral palsy and Alzheimer's disease (e.g., Serruya & Kahana, 2008). The impact (‘Consequences’) of the Diagnoses on cognitive functioning, independence and quality of life are other emerging topics.

In terms of the ‘Populations’ included in the reviewed studies, ‘Children’ are the most referred of all. ‘Adolescents and Youths’, ‘Adults’ and ‘Older Adults’ are also mentioned, along with calls of attention to the prolonged developmental trajectory of the pathologies that result in cognitive dysfunction in general and, especially, in executive dysfunction. Some references to ‘Animal’ studies also appear, as well as to a study that addresses cultural specificities.

The theoretical models identified in the literature have attempted to explain cognitive functions (e.g., ‘Memory’, ‘Attention’) and disorders (e.g., Autism Spectrum Disorders), and to provide a foundation for assessment or intervention practices (e.g., the basis for motivational interviewing). Although, some references to the models only allow their allocation to a more general category, such as ‘Neuropsychological Models’. Regarding executive function models (as part of ‘Neuropsychological Models’, the analysis reveals that EF are viewed as including different processes and sub-processes. EF is conceived as a supervisory capacity for directing more modular or specific processes. Thus, it is viewed as resulting from the combination of cognitive (e.g., working memory, inhibitory control), emotional and behavioral processes, and this is reflected in the diversity of models. Examples of often mentioned EF models are Mark Ylvisaker’s and Norman and Shallice’s models.

In terms of ‘Central Nervous System’, a constellation of ‘(Dys)Functions’ is reported. They are mostly ‘Cognitive (Dys)Functions’, though ‘Behavioral’, ‘Social’, ‘Motor’ and ‘Physical (Dys)Functions’ also emerge, and often occur concomitantly. As expected under the current search, the most mentioned cognitive dysfunctions refer to ‘EF’. However, dysfunctions of ‘Memory’ and ‘Attention’, among others, are also represented. Several works present EF ‘Terminology’ (executive function(s), executive functioning, and executive dysfunction are the most referred terms in the reviewed literature), as well as EF ‘Components’ (sub-processes).

In addition to ‘(Dys)Functions’, different ‘Structures’ of the ‘Central Nervous System’ are mentioned. In the case of EF, different sub-processes are associated with specific brain regions, especially different regions in the (pre)frontal cortex: the dysfunctions may result from either direct damage of the (pre)frontal lobes or from the disruption of their connections to other brain regions. In fact, there is growing recognition about the importance of the interconnectivity between different brain regions and of their active role in EF (distributed neuronal system). The articles also refer ‘Types of Lesions’, namely in (pre)frontal regions of the brain, and their ‘Consequences’.

Regarding ‘Assessment’, the vast majority of studies refer ‘Neuropsychological’ assessment through standardized psychometric measurements administered in controlled environments, such as the laboratory, or in clinical settings. To a lesser degree, ‘Neurologic’ evaluations are also mentioned, through instruments known as neuroimage techniques, including TMS, fMRI, PET, EEG, and MEG. 'Physical' and 'Behavioral' evaluations also appear. The reviewed studies report 'Limitations' of traditional instruments of neuropsychological assessment: for not considering the complex nature of EF, the diversity of sub-processes involved, the specificity of pathologies associated with EF, the necessity of ecological evaluations, the developmental stage of the subjects under evaluation, or the consequences of repeated evaluations, namely learning. Various works propose ´Recommendations' to overcome some of the previously mentioned limitations, such as alternative procedures to assessment. Other works propose new 'Instruments' and test their 'Validity'. The ´Professionals' referred as being involved in assessment are clinicians, clinical neuropsychologists, psychologists or practicing physicians.

In terms of 'Intervention', most treatments pertain to the 'Cognitive Rehabilitation' 'Type'. Like in assessment, studies highlight intervention 'Limitations', such as little consideration of rehabilitation for the specificities of pathologies or for the developmental stage in which the intervention occurs, lack of patient involvement in the therapeutic process, in part as a result of their limited awareness of their deficits, or methodological issues related with the assessment of intervention effects. Works also include new and promising methodologies that have been used as a means to overcome the limitations of traditional interventions, but which still need further research. In fact, several articles offer 'Recommendations', such as additional development of rehabilitation tools, availability of integrated and holistic services, refinement of rehabilitation techniques, interventions that consider the real-world context, development of transdisciplinary teams, or the use of supportive devices and/or emerging treatments, such as virtual reality environments. The need for further evaluation of these new treatments in systematic trials is also mentioned. The works provide specific 'Strategies' and 'Instruments' to be used in intervention, aiming to increase the potential for generalization of the learned skills. The 'professionals' referred point to the importance of multi-, and transdisciplinary teams.

Conclusions

The scientific production on EF conveys the complexity of this topic, dispersed in a variety of objects of study – from theoretical models attempting to explain these (dys)functions to issues of terminology. The sheer variety of themes associated with EF called for a systematization of the current information around this topic, which constituted the goal of this literature review.

The analysis revealed the current interest in the theme, reflected in the growing number of publications in this area over the years. The following themes emerge in the publications: (1) the different populations with diverse diagnoses, from children to the elderly, or even animals, and the importance of considering the specificities of developmental stages in assessment and intervention practices, (2) "theoretical models" that attempt to explain the cognitive functions or the proposed interventions, (3) the variety of (dys)functions associated to EF, frequently reflecting structural or functional frontal pathology, (4) the diversity of cognitive processes connected to EF, such as attention and memory, (5) the neuroanatomical correlates of (dys)functions, showing the specialized involvement of the prefrontal cortex, with specific regions mediating different sub-processes and the inclusion of other traditionally less considered regions (e.g., posterior cortical and subcortical regions), suggesting that EF are mediated by dynamic *networks*, and that the prefrontal cortex is a heterogeneous neuroanatomical region, (6) the difficulties inherent to "assessment" and "intervention", and (7) the proposal of new instruments and strategies of assessment and intervention, and, frequently, recommendations for future work in these domains, revealing the evolution of the theme.

Despite the interesting advances in the last years, EF need more research and further development. Reviewed works suggest future directions for research, pointing to the need of well-controlled studies to include more naturalistic and ecologically valid tasks. More comprehensive assessment of post-injury changes in daily functioning and of the effectiveness of interventions is needed. Focus on the generalization of acquired skills to everyday life, improving promising rehabilitation techniques and applying evidence to clinical practice seem to be future trends. New technologies, particularly in the domain of neuroimaging, as functional MRI, may be a crucial contribution, adding evidence to neuropsychological human and animal studies.

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II. Desenvolvimento, Implementação e Avaliação do *Computer-Assisted Rehabilitation Program - Virtual Reality* (CARP-VR)

Artigo 3 - O Desenvolvimento de um Programa de Reabilitação Cognitiva com Recurso a Tecnologias Informáticas

Dores, A. R., Carvalho, I., & Castro-Caldas, A. (2009). *O desenvolvimento de um programa de reabilitação cognitiva com recurso a tecnologias informáticas*. Proceedings of "VII Simpósio Nacional de Investigação em Psicologia". Braga, Portugal, 645-659.

O Desenvolvimento de um Programa de Reabilitação Cognitiva com Recurso a Tecnologias Informáticas

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Resumo

Numa era em que proliferam as tecnologias informáticas parece inegável que os serviços de reabilitação neuropsicológica não podem ficar alheios a esta realidade. O Computer-Assisted Rehabilitation Program – Virtual Reality (CARP-VR) está a ser desenvolvido por uma equipa multidisciplinar, como um programa que visa a reabilitação das funções executivas em pacientes com lesão cerebral adquirida. Este programa combina princípios básicos da reabilitação cognitiva com tecnologia inovadora, designadamente a realidade virtual. Procura ainda constituir-se uma ferramenta adaptada às especificidades de diferentes doentes, incorporando soluções que aumentam a possibilidade de participação no referido programa. A crescente facilidade no desenvolvimento de ferramentas de reabilitação que recorrem a tecnologias informáticas não dispensa uma forte integração teoria-prática e uma análise crítica sobre os resultados, ambas aqui consideradas. Neste trabalho apresentamos o processo de desenvolvimento de um programa de reabilitação a partir da literatura existente e do projecto em curso, evidenciando a importância da tecnologia no domínio da reabilitação cognitiva.

Palavras-Chave: Reabilitação Cognitiva, Realidade Virtual, Processo de Desenvolvimento.

1. OBJECTIVOS[8]

Neste trabalho propomos um modelo de Processo de Desenvolvimento de um Programa de Reabilitação com recurso à tecnologia de realidade virtual (RV), a partir da literatura existente e de um projecto em curso, o Computer-Assisted Rehabilitation Program – Virtual Reality (CARP-VR) (Dores *et al*., 2009a, 2009b), evidenciando a importância das novas tecnologias no domínio da reabilitação cognitiva. A experiência e aprendizagem que têm decorrido do desenho e desenvolvimento do nosso projecto justificam esta proposta de um modelo organizador desse processo.

Com a sua elaboração procuramos oferecer informações e orientações úteis acerca desta temática aos profissionais na área da reabilitação cognitiva, no sentido de estimular o seu interesse pelo desenvolvimento de ferramentas de reabilitação e/ou facilitar a selecção entre as que existem no mercado, caso optem pela sua aquisição. Consideramos que este artigo pode ainda ser útil a profissionais da área da Engenharia Computacional, que ao trabalhar no desenvolvimento destas ferramentas possam sentir dificuldade em perceber as reais necessidades dos futuros utilizadores dos seus produtos.

2. DESENVOLVIMENTO DO TEMA

Apesar dos avanços científicos, sociais e políticos dos dias de hoje, assistimos, nas sociedades contemporâneas, a uma realidade diária frequentemente silenciosa (Santos, de Sousa & Castro-Caldas, 2003; SPAVC, 2006), contudo, com severas consequências negativas. Referimo-nos às Lesões Cerebrais Adquiridas (LCA), resultado de Traumatismos Cranio-Encefálicos (TCE) ou de doenças neurológicas, como os Acidentes Vasculares Cerebrais. No caso dos TCEs, crianças, idosos e, fundamentalmente, jovens adultos, com plena capacidade produtiva, vêem as suas vidas interrompidas como consequência de acidentes de viação ou de trabalho. Independentemente da causa, as consequências tendem a reflectir-se a nível pessoal, familiar e social. Cada doente apresenta uma combinação de problemas única e complexa, envolvendo défices físicos, cognitivos, emocionais, psicossociais e vocacionais duradouros (Lezak, 2004; Sbordone, Liter, Pettler-Jennings, 1995).

Nas últimas décadas, registaram-se em Portugal progressos muito significativos ao nível das políticas e das práticas dirigidas às pessoas com deficiências e incapacidades. Apesar disso, do total desta população, a taxa de utilização dos serviços disponibilizados

[8] As referências bibliográficas deste artigo encontram-se no formato proposto pela revista em que foi publicado.

pelo sistema de reabilitação português é apenas de 32% (CRPG & ISCTE, 2007; Guerreiro *et al.*, 2008). Além disso, embora se verifique um número crescente de pessoas com deficiências e incapacidades adquiridas ao longo da vida, a grande maioria das estruturas do sistema de reabilitação é dirigida às deficiências congénitas.

Estes dados evidenciam a necessidade de serviços adequados e orientados para as reais necessidades desta população. Tal implica a recuperação do paciente, ao mais alto nível de adaptação física, psicológica e social. Isto inclui todas as medidas direccionadas à redução do impacto das condições incapacitantes, ajudando as pessoas afectadas a conseguirem uma máxima integração social (Wilson, 1997).

Atendendo à natureza específica e à complexidade das incapacidades resultantes da lesão, um programa de reabilitação beneficia de intervenções holísticas e interdisciplinares, que atendam ao contexto de desenvolvimento de cada doente. Porém, são muitas as exigências com que se vêem defrontados os doentes, as suas famílias e os profissionais, como a ausência de consciência dos défices, as dificuldades de motivação, a necessidade de uma reabilitação sustentada pelos resultados prévios e de realização em contexto, os progressos lentos, ou mesmo a crença muitas vezes irrealista da possibilidade de retorno ao nível de funcionalidade e ao projecto de vida anterior. A estas dificuldades acrescem a falta de recursos humanos e de ferramentas para fazer face às exigências referidas (Guerreiro *et al.,* 2008).

Assim, resultado da incapacidade de resposta dos serviços ou da insatisfação com os serviços prestados, muitos dos doentes vítimas destas condições não usufruem de programas de reabilitação neuropsicológica e de reabilitação cognitiva em particular. Tal reflecte-se frequentemente no afastamento do contexto laboral, o que contribui para perpetuar um ciclo de exclusão e situações de dependência (CRPG & ISCTE, 2007).

A RV revela-se uma tecnologia promissora na prossecução destes objectivos (Rizzo & Wiederhold, 2006; Rose, Brooks & Rizzo, 2005). O projecto CARP-VR que serve de base à elaboração deste trabalho, como já foi referido anteriormente, decorre da necessidade de criação de ferramentas inovadoras para fazer face às exigências da reabilitação cognitiva de doentes com Lesão Cerebral Adquirida, particularmente relacionadas com o funcionamento executivo. Tais necessidades são sinalizadas na literatura, onde se pode constatar, nas últimas décadas, a emergência de programas de reabilitação com recurso a tecnologia de RV, como forma de tentar ultrapassar as principais limitações das intervenções tradicionais (e.g., a RV pode permitir o desenvolvimento de ambientes de aprendizagem seguros que superem as dificuldades de levar estes doentes para contextos reais) (Castelnuovo *et al*., 2003). No entanto, os ambientes virtuais (AVs) existentes, de modo geral, não se encontram adaptados à realidade portuguesa, podendo condicionar quer o realismo das situações, quer a generalização das competências adquiridas, e poucos se dedicam às funções executivas (Standen *et al*., 2000; Hilton *et al*., 2002; Rizzo *et al*., 2002; Parsons & Rizzo, 2008).

Além disso, o facto de mesmo doentes com bom desempenho em testes neuropsicológicos de avaliação das funções executivas apresentarem disfunção em actividades de vida diária, torna a avaliação através de instrumentos psicométricos e algumas metodologias de intervenção tradicionais processos questionáveis (Evans, 2003; Shallice & Burgess, 1991). O número crescente de publicações neste domínio parece revelar a consciência da necessidade de ferramentas de avaliação e de reabilitação cognitiva inovadoras e com maior validade ecológica.

O CARP-VR consiste em AVs nos quais é possível resolver tarefas de vida diária, em condições de segurança, recorrendo a estratégias de reabilitação neuropsicológica estabelecidas. A organização do programa por níveis de dificuldade para a progressão dos doentes, a inclusão de um editor de mapas e o uso de interacção multimodal (por exemplo, comando motor e verbal) podem ser consideradas vantagens, ao permitirem alterar os AVs de acordo com as necessidades da intervenção e expandir a utilização do programa a uma maior diversidade de doentes.

Perante os objectivos de conceptualização, desenvolvimento e implementação de um programa de reabilitação cognitiva com recurso à tecnologia de RV, colocamo-nos as seguintes questões: Quais os passos para desenhar um programa cognitivo de reabilitação teoricamente fundamentado? E quais os passos para desenhar um programa cognitivo de reabilitação RV? Da revisão da literatura efectuada, destacaremos os modelos que assumiram um papel mais relevante na estruturação do nosso trabalho.

Sohlberg e Mateer (1989) põem em evidência a ruptura entre o exercício de actividades de reabilitação muitas vezes sem o conhecimento teórico da relação cérebro-comportamento e entre as que, por sua vez, dispõem do conhecimento teórico, mas frequentemente se encontram afastadas do exercício profissional, da prática nessa área. Indicam ainda não existirem na literatura muitas sugestões sobre como resolver esta situação. Dada esta discrepância, como conseguir o desenvolvimento de programas efectivos?

Cremos que as mudanças a que se tem assistido na última década ao nível da formação, concretamente no perfil de saída dos profissionais nesta área, e o investimento cada vez maior na aprendizagem ao longo da vida, muitas vezes a nível pós-graduado, podem contribuir para o desenvolvimento de programas de reabilitação cognitiva suportados por princípios neuropsicológicos. Isto na medida em que os profissionais da prática podem ter hoje uma melhor formação teórica acerca desta temática. Paralelamente, o desenvolvimento destes programas beneficiará certamente com a constituição de equipas inter e multi-disciplinares em que se reúnam conhecimentos acerca da cognição, do funcionamento do cérebro, das consequências das lesões e dos mecanismos de recuperação, bem como das actividades promotoras da reabilitação das funções cognitivas afectadas (Psicologia Cognitiva, Neurologia e Neuropsicologia). São ainda indispensáveis conhecimentos acerca do desenvolvimento desses programas a nível da programação e da modelação (Engenharia). Assim, a estreita relação entre a teoria (conhecimento da relação cérebro-comportamento) e a prática (experiência decorrente da intervenção) favorecerá o desenvolvimento de programas teoricamente fundamentados.

Os mesmos autores (Sohlberg & Mateer, 1989) propõem um modelo que pode auxiliar na resposta à primeira questão: o *process-specific approach to cognitive rehabilitation*, que postula que áreas cognitivas específicas podem ser retreinadas e "remediadas", ainda que nem sempre a um nível funcional. Este modelo aposta na restauração da função, assim como em técnicas de compensação que beneficiem os doentes em dificuldades residuais. O modelo propõe três fases para o desenho de programas de reabilitação cognitiva teoricamente fundamentados: fase da recolha de informação; fase do desenvolvimento do programa e fase da avaliação da eficácia. A primeira deve envolver quatro passos: rever literatura da Psicologia Cognitiva e da Neuropsicologia, examinar a prática de "remediação" clínica e observar doentes com défices cognitivos. A segunda fase refere-se à delineação das componentes teóricas relativas às áreas dos processos cognitivos e ao desenho das tarefas de tratamento, organizadas hierarquicamente para cada componente do modelo teórico. Por último, a terceira fase envolve a realização de ensaios clínicos com os doentes com lesão cerebral para quem foi concebido o programa.

No que concerne à resposta à segunda questão, Costa (2000) efectua uma revisão de trabalhos que estruturam procedimentos para o desenvolvimento de AVs, analisando as suas potencialidades e limitações. A própria autora propõe ainda um modelo com este fim, estruturado em quatro etapas: Levantamento de requisitos, que consiste na análise e definição dos requisitos do ambiente; Projecto, em que se definem as tecnologias a serem utilizadas e o comportamento dos objectos; Implementação, em que se define a construção das cenas e dos objectos 3D que as integram; e Avaliação, em que se testa o ambiente, verificando possíveis problemas e o seu valor na área de aplicação.

De modo mais específico, relativamente ao desenvolvimento do seu programa AVIRC (Ambientes Virtuais na Reabilitação Cognitiva de Pacientes Neurológicos e Psiquiátricos), Costa (2000) propõe as seguintes etapas: 1. visão geral do AVIRC (1.1 motivação, 1.2 objectivo do ambiente, 1.3 arquitectura funcional); 2. desenvolvimento (2.1 definição dos requisitos – definição dos usuários, tarefas e interacções; definição dos requisitos gerais, definição dos requisitos específicos; 2.2 projecto: definição das tecnologias de entrada, saída e de armazenamento; definição das tecnologias de *software* e *hardware*; modelagem dos objectos, comportamentos e interacções; 2.3 implementação – definição e preparação das imagens, dos objectos e sons; construção do AV; 2.4 avaliação – avaliação do desempenho; avaliação da usabilidade e do valor da aplicação); 3. Experimentação (exploração da aceitação da tecnologia de RV e da motivação).

Mais recentemente, Castelnuovo e colaboradores (2003) propõem uma lista de questões, respostas possíveis, e indicações para os desenhadores de AVs. Destacamos, a nível deste último tópico: o desenvolvimento de AVs que assegurem apenas o nível (e a qualidade) de presença que cada aplicação requer; o realismo dos ambientes; e situações ecológicas que envolvam interactividade.

Seguidamente apresentamos o nosso modelo de Processo de Desenvolvimento de um Programa de Reabilitação RV, proposta que sustenta o desenvolvimento do CARP-VR a partir da revisão da literatura, da consulta de especialistas e da incorporação de alterações decorrentes do refinamento do próprio processo (cf. Figura 1).

O desenvolvimento do Programa de Reabilitação RV deve começar com a Revisão Teórica e Reflexão acerca das Práticas (Tarefa 1), de acordo com os passos 1 a 4 do Modelo de Sohlberg e Mateer (1989), ponto de partida para o Desenho Conceptual (Tarefa 2). Na Tarefa 2, os psicólogos membros da equipa multidisciplinar apresentam os requisitos do programa (designadamente, quais os AVs, as actividades a desenvolver em cada ambiente, o número de níveis de dificuldade de cada ambiente) tendo em conta a especificidade da população estudada, de acordo com os passos 5 e 6 do Modelo de Sohlberg & Mateer (1989), e os engenheiros da equipa contribuem com sugestões para a operacionalização desses requisitos. Para o Desenvolvimento da Aplicação de Interacção (Tarefa 3), é especificado o modo de interacção dos doentes com o programa, baseado no conhecimento dos psicólogos acerca das características destes doentes e nas soluções técnicas por parte da Engenharia. Para o Desenvolvimento dos Ambientes Virtuais (Tarefa 4), são especificados os AVs. Por último, é ainda especificada a metodologia do estudo piloto e do estudo experimental a realizar e os eventos de divulgação do programa (Tarefas 7 a 11). Na Tarefa 2, procede-se igualmente à especificação do equipamento necessário às diversas fases do processo.

No que concerne à articulação entre as diferentes tarefas, o Desenho Conceptual (Tarefa 2) é uma actividade contínua ao longo do projecto, requerendo a revisão da literatura de modo continuado, a consulta de peritos (nomeadamente neurologistas) e a elaboração de relatórios que orientem a realização das tarefas seguintes. Da Tarefa 3

(Desenvolvimento da Aplicação de Interacção) deverá resultar a aplicação computacional. Esta envolve o desenho e implementação do sistema de navegação (e.g., *joystick*, teclado, sistema de reconhecimento de voz, etc.). Envolve igualmente o desenho e a implementação do motor gráfico e do sistema de reprodução áudio. Além destes componentes, nesta tarefa será desenvolvida a interface de gestão dos pacientes e a base de dados dos resultados (a partir da qual será fornecido *feedback* aos doentes).

Na tarefa 4, o objectivo é o Desenvolvimento dos Ambientes Virtuais (e.g., cidade, loja, …) onde os pacientes realizarão actividades baseadas nas tarefas de vida real (envolve o desenho visual e do som). Sugerimos que o seu desenvolvimento ocorra por fases, em articulação com a Tarefa 3, e de acordo com o especificado na Tarefa 2.

A integração dos produtos das Tarefas 3 e 4 dá origem a modelos que vão sendo testados progressivamente à medida que vão sendo concluídos (Tarefa 5), permitindo detectar eventuais falhas com o objectivo da sua correcção imediata e aprendizagem a aplicar nas fases seguintes. Por sua vez, a Integração do Programa de Reabilitação (Tarefa 6) consiste na integração dos diversos modelos, dando origem ao protótipo final. Assim, os sistemas (motor gráfico e sistema de interacção) encontrar-se-ão integrados com o *hardware* de visualização seleccionado (Tarefa 3) e com o desenho visual e de som (Tarefa 4). Na etapa final desta tarefa deve ocorrer o acompanhamento e supervisão dos produtos (protótipos) na tarefa de teste, de modo a ocorrerem todas as alterações que se revelem relevantes.

Para além do teste realizado com sujeitos sem deficiência/incapacidade, para avaliação do equipamento, uma amostra de pacientes voluntários deverá igualmente testar o(s) protótipo(s) final(is). Este procedimento permite envolver os futuros utilizadores no desenvolvimento do produto, visando a construção de um sistema de uso fácil e adequado. Assim, eventuais ajustes ao programa resultarão de informação fornecida por estes sujeitos (bem como pelos sujeitos sem deficiência/incapacidade) antes da intervenção propriamente dita.

Posteriormente, a satisfação, a motivação com a utilização do CARP-VR e os efeitos da intervenção serão avaliados através de um estudo piloto (a nível do desempenho nas tarefas, das funções cognitivas seleccionadas, da funcionalidade em tarefas de vida real dependentes dessas funções e da generalização das competências adquiridas) (Tarefa 7 – Intervenção: Estudo Piloto e Tarefa 8 – Avaliação).

Para este estudo piloto, o contacto dos pacientes com o programa deve começar por uma sessão de familiarização com a tecnologia de RV e com os objectivos e funcionalidades do mesmo. A seguir, os pacientes devem começar pelo nível mais ajustado às suas capacidades actuais. A progressão no programa será determinada pelo desempenho dos sujeitos nas actividades.

Subsequentemente, em função dos resultados obtidos no estudo piloto, deverá ocorrer a intervenção junto de uma amostra maior, concretamente, junto de um grupo experimental e um de controlo que permita validar os efeitos da intervenção (Tarefa 9 – Intervenção: Estudo Experimental), recorrendo-se com este fim a diversas estratégias de avaliação, designadamente avaliação neuropsicológica e/ou ressonância magnética funcional, entre outras (Tarefa 10 – Avaliação). As Tarefas 8 a 10 do nosso modelo respeitam as indicações dadas pelo passo 7 do Modelo de Sohlberg & Mateer (1989).

A Tarefa 11 consiste na Conclusão do projecto, envolvendo diferentes actividades de divulgação do projecto e dos resultados obtidos (e.g., reuniões científicas) e a elaboração do relatório final.

A Gestão do Projecto (Tarefa 0) deve ocorrer de forma contínua ao longo de todo o projecto. Consiste na coordenação de todas as tarefas, envolvendo a sua articulação e a dos membros da equipa intervenientes em cada tarefa. Deve ainda incluir a supervisão, através de reuniões com os responsáveis por cada uma das tarefas e a partir dos relatórios de progressão.

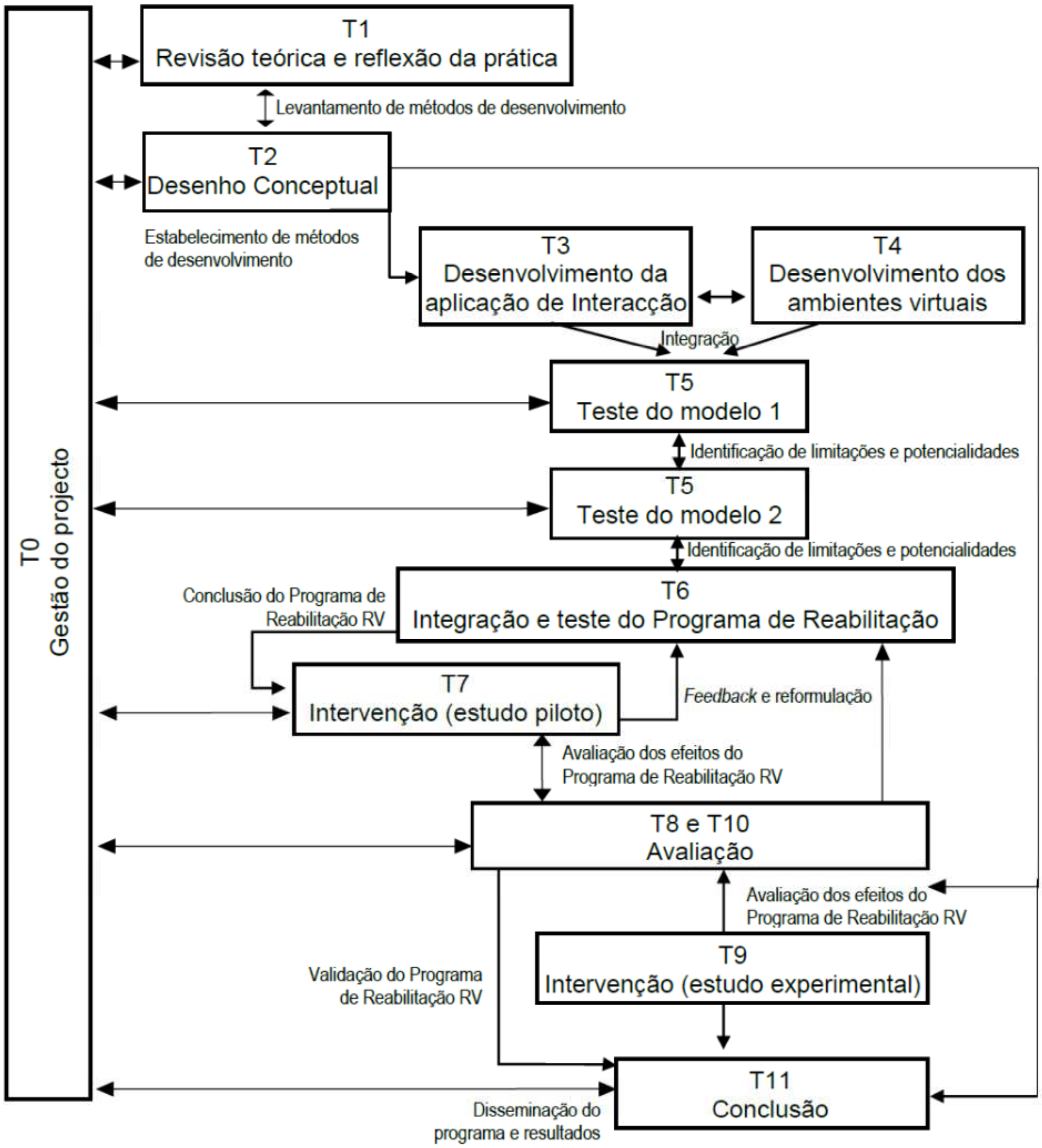

Figura 1 - Proposta de desenvolvimento de um Programa de Reabilitação RV

3. DISCUSSÃO

Nesta proposta, procuramos conciliar preocupações relativas ao desenvolvimento de um modelo de reabilitação cognitiva fundamentado teoricamente com as especificidades do desenvolvimento de um Programa em RV (por exemplo, as Tarefas respeitam as indicações do Modelo de Sohlberg e Mateer, 1989). Procuramos ainda conservar as principais potencialidades dos modelos revistos.

A participação num programa de reabilitação neuropsicológica obriga, não raras vezes, ao confronto da imagem que os doentes têm de si e das suas capacidades com a imagem do que são no presente. Este é um momento difícil que pode revelar-se inevitável e ter implicações para a construção de um novo projecto de futuro, ajustado às reais capacidades, que a reabilitação procurará potenciar ao máximo. Sem a consciência dos défices os doentes dificilmente valorizam a necessidade da reabilitação e se motivam a permanecer neste processo face às dificuldades que lhe são inerentes, como os progressos serem lentos, a intervenção prolongada, terem pouca relação com as actividades de vida real, entre outras (Guerreiro *et al*., 2008).

Considerando estas limitações, o desenvolvimento de programas de reabilitação cognitiva deve, para além de promover a melhoria do desempenho nas tarefas do programa e a reabilitação da função ou funções cognitivas seleccionadas, fomentar a satisfação e a motivação dos doentes nas actividades de reabilitação. Os programas de Reabilitação em RV podem desempenhar uma função importante neste sentido.

Com estes programas, espera-se que as competências adquiridas se generalizem para as actividades de vida real, reflectindo-se na melhoria da independência funcional dos doentes, na sua qualidade de vida e, desejavelmente, no retorno à vida activa. A RV pode revelar-se uma tecnologia promissora na prossecução destes objectivos.

Para que isso se verifique, parece-nos igualmente importante conseguir o envolvimento e interesse dos profissionais que diariamente se dedicam à actividade da reabilitação. Cremos que o seu envolvimento será favorecido pela desmistificação da ideia de que a tecnologia veio para substituir os profissionais.

Mesmo que com o desenvolvimento deste tipo de ferramentas também se pretenda maximizar os serviços prestados, fazendo-os chegar a uma população mais alargada, e responder a uma política de contenção orçamental, não existe por si só nada de inerentemente terapêutico num computador. Ainda que a reabilitação baseada em computadores possa oferecer vantagens distintas em relação a técnicas de reabilitação não computorizadas (Matthews, Harley & Malec, 1991; O'Connor & Cermak, 1987), particularmente no caso da tecnologia de RV (Castelnuovo *et al*., 2003), a função dos profissionais estará sempre longe de colocar um doente em frente a um computador. É crucial que assumam uma postura crítica perante programas de reabilitação cognitiva comerciais ou auto-concebidos, questionando-se acerca dos seus efeitos e papel na intervenção.

Por exemplo, Diller e Gordon (1981) sugerem a resposta a uma lista de questões que poderão ajudar a este fim, como: "Quais os défices cognitivos que estão a ser tratados? De que modo são os défices operacionalizados em termos mensuráveis? Qual é o estímulo que desencadeia o défice e de que modo pode ser manipulado para se tornar mais fácil ou mais difícil? Quais são as respostas que servem como indicadores do défice? Qual é o conteúdo do tratamento? Como é administrado o programa? Com que frequência? Quais são os critérios estabelecidos para continuar, alterar ou parar o programa?

Ao profissional de reabilitação competirá sempre planear a intervenção, utilizar o programa de RV como suporte para objectivos de tratamento específicos delineados por si, colaborar na análise dos resultados do desempenho juntamente com o doente e considerar a reabilitação assistida por computador como uma das tarefas terapêuticas (Sohlberg & Mateer, 2001). Tal deve ocorrer mesmo nos casos em que o programa de reabilitação seja fornecido à distância, via Internet, por exemplo a populações que, em condições normais, se veriam privadas deste tipo de serviços.

4. CONCLUSÕES

Nas últimas décadas assistimos a um aumento considerável de ambientes em RV desenvolvidos, particularmente na Medicina, na Educação e, mais recentemente, no domínio da reabilitação. Contudo, a conceptualização, desenvolvimento e implementação de um programa de reabilitação cognitiva, particularmente com recurso à tecnologia de RV é um processo exigente e demorado, feito de avanços e retrocessos que esperamos ajudar a minimizar com este trabalho.

A diversidade individual na recuperação espontânea, a natureza, a localização e magnitude da lesão, o tempo pós-ocorrência, a idade dos sujeitos ao nível de funcionamento pré-morbido, o consumo de substâncias, o nível sócio-educacional e a presença de perturbações psicológicas são variáveis que podem influenciar os resultados obtidos. A dificultar a realização de projectos neste domínio surgem ainda questões éticas e os elevados custos do equipamento e do desenvolvimento. Apesar disso, mas fundamentalmente por tudo isso, cada profissional no domínio da reabilitação tem um papel, um contributo a dar de modo a potenciar o desenvolvimento desta área (Sohlberg & Mateer, 2001).

A proposta que aqui apresentamos, ao mesmo tempo que procura ser simples no sentido de estimular à sua replicação, procura igualmente ser abrangente, na medida em que envolve as etapas desde a concepção/desenho fundamentado até à disseminação dos resultados, com objectivos de transformação da prática. Finalizamos realçando que não se pretende com este trabalho fornecer uma receita, por tudo o que referimos anteriormente, mas tão só uma metodologia possível baseada no nosso trabalho em curso. Como terá respondido Thomas Edison, quando questionado como se sentia depois de ter fracassado incontáveis vezes na tentativa de fabricar uma lâmpada, afirmamos «Eu nunca fracassei, muito pelo contrário. Consegui descobrir, com grande êxito, milhares de procedimentos de como não fabricar uma lâmpada».

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Artigo 4 - Virtual Reality: Application to Cognitive Rehabilitation After Acquired Brain Injury

Dores, A. R., Carvalho, I., Abreu, C., Nunes, J., Leitão, M., & Castro-Caldas, A. (2009). *Virtual Reality: Application to cognitive rehabilitation after acquired brain injury*. In K. Blashki (Org.), DSAI 2009: Proceedings of the 2nd International Conference on Software Development for Enhancing Accessibility and Fighting Info-Exclusion Lisboa. Lisboa: DSAI, 31-36.

Virtual Reality: Application to Cognitive Rehabilition After Acquired Brain Injury

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Abstract

Acquired brain injury (ABI) is one of the main causes of death and disability in Portugal and other Western countries. ABI typically results in physical, cognitive and psychosocial deficits, leading to life-long dramatic changes in the quality of life (QOL) of patients and their families, with well-documented negative implications for their community integration. Independent mobility using means of transportation is considered a nuclear area of community integration for people with disabilities [3]. However, direct contact with reality is limited for this population. Virtual reality (VR) constitutes a promising alternative of approximation to real life that may help increase the level of generalization of skills developed in programs that use this kind of technology. However, research on VR effects is necessary. The main goal of our project is to study the use of VR technology in the rehabilitation of executive dysfunction and memory. A VR program, CARP-VR, is in development, consisting of environments that simulate reality, with which patients will interact, performing various tasks. It is expected that CARP-VR intervention will lead to cognitive gains and generalization of acquired capacities to real-life activities, reflecting an amelioration of patients' functional independence and QOL that will contribute for the integration of these patients.

Keywords: Acquired brain injury, Cognitive rehabilitation, Virtual reality.

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INTRODUCTION[10]

Acquired brain injury (ABI), resulting from traumatic brain injury (TBI) and from neurological diseases such as stroke, is one of the main causes of death and disability in Portugal and other Western countries. However, due to the advances in medical technology and in emergency services, TBI and stroke-related mortality has decreased [1]. Coupled with the fact that TBI typically occurs in young adults, resulting in physical, cognitive and psychosocial deficits, this means life-long dramatic changes in the quality of life (QOL) for patients and their families, with well-documented negative implications for their community integration [2][3]. A study indicated that, of the people admitted to a hospital, 1/3 will have TBI sequelae, 20% severe, 80% mild [4]. Today, this would correspond to some 2500 new cases per year with mild or severe limitations [5]. Rehabilitation interventions that promote the return to an active life and increase patients' QOL are crucial. This subject was presented and discussed in a recent issue of the newspaper Público, in an article with the headline "Há vida depois de um coma", ("There's life after a coma"), revealing social recognition of the impact of this condition, ignored for so many years due to patient isolation and deficits and treatment extent, that make reintegration so difficult, and encouraging a proactive, rather than a passive, attitude in the face of the challenges posed by this condition [6].

Deficits in ABI will have underlying brain mechanisms that have been affected. To develop effective programs of cognitive rehabilitation, and to know the brain mechanisms involved in this process represent major contributions for research, as well as for practice in this area. Knowing the brain mechanisms at work in cognitive rehabilitation will help improve intervention programs, but the studies in this domain are still incipient.

NEUROPSYCHOLOGICAL REHABILITATION

Given the difficulties associated with ABI, that can include: Medical difficulties, altered sensory abilities, impaired physical abilities, impaired ability to think and learn, altered behaviour and personality or impaired ability to communicate, neuropsychological rehabilitation can provide tools to help find a life compromise and the lost life style by developing physical, mental, and sensorial capacities and diminishing limitations through technical assistance and integration of multidisciplinary knowledge [7]. When functionality and problem-solving ability are significantly impaired due to dysfunction at the level of memory and executive functions (EF), cognitive rehabilitation becomes particularly

[10] As referências bibliográficas deste artigo encontram-se no formato proposto pela revista em que foi publicado.

important. EF refers to cognitive capacities involved in initiating, planning, sequencing, organizing, and regulating behavior [8] indispensable to the most basic tasks of daily life such as independent mobility or supermarket shopping. In fact, at the cognitive level, impaired memory and executive dysfunction are two of the most pervasive and disabling consequences of brain damage [9]. Despite the fact that they should be a major target of interventions, they continue to be major barriers to the return to normal life in neurological patients, because the development of cognitive rehabilitation has not accompanied the significant advances observed in other services targeted at this problem.

Still, some advances have been made. A recent study indicates, “There is now a substantial body of evidence demonstrating that patients with Traumatic Brain Injury or stroke benefit from cognitive rehabilitation” and, “Future research should move beyond the simple question of whether cognitive rehabilitation is effective, and examine the therapy factors and patient characteristics that optimize the clinical outcomes of cognitive rehabilitation” [10].

As mentioned before, for EF difficulties may be greater because, in spite of the devastating effect it can have, less attention has been paid to it in scientific literature than to other cognitive functions. A review by Dores (2006) identified some reasons for this, such as lack of theoretical consistency about EF’s nature, diversity of deficits associated to it, patients’ limited awareness of their incapacity, inexistence of clearly effective rehabilitation programs, and issues of instrument validity [11]. The deficits in this process may affect activities such as independent mobility using means of transportation, considered a nuclear area of community integration for people with disabilities [12]. However, direct contact with reality is limited, for this population. Existing solutions do not allow the variety and frequency of individual participation that professionals consider acceptable [13]. Also, navigation for TBI patients is affected when no proximal clues are present, perhaps highlighting the fact that their deficits are due to difficulties in forming, retrieving, or using cognitive maps [14].

Regardless of the functions affected, literature today advocates holistic interventions that go beyond cognitive limitations to promote deficit awareness, development of compensatory strategies, and vocational counseling [15]. An example of this is the program developed in our country at the Centro de Reabilitação Profissional de Gaia. Yet, cognitive rehabilitation remains a significant challenge for professionals in this area. Even if part of broader protocols, it calls for structured intervention programs and evaluation methods that are effective.

NEW TRENDS BROUGHT BY VR

Traditional instruments, including non-VR computer programs, used in EF intervention have been criticized for their lack of relation with patients' past experience [16]. Such disconnect may lead to the recognized low generalization to real life of competences gained in training, and to decreased motivation in tasks.

New and promising methodologies have been used as a means to overcome the limitations of traditional interventions [17]. In the past few years, virtual reality (VR) technology began to be employed in intervention and evaluation, having received increased interest for its recognized potential in this area [18][19]. It allows the development of safe learning environments that overcome the difficulties of taking these patients to real environments. It also implements several aspects that literature has identified as effective: Self-training and learning, use of "game" factors to promote motivation, and possibility of immediate feedback [20]. It further allows the possibility of programming task difficulty in function of patients' evolution, or contingent to success, and above all, of adapting the environments to patients' characteristics (a major criticism to traditional interventions [21], as is already done in Portugal in other domains, such as phobia treatment [22]. Results from these studies with VR technology have been promising, and the authors have concluded in favor of using VR in combination with standard psychotherapy in the treatment of acrophobia [23].

A review of initial studies on the potential of VR for rehabilitation of different cognitive processes (e.g., executive function, memory, spatial capacity) shows very encouraging results [24]. However, most reviewed studies developed environments that are versions of neuropsychological tests for purposes of evaluation. Yet, it is possible to develop innovating virtual environments with rehabilitation functions, like those for treating Post-Traumatic Stress Disorder [25]. In Portugal two different pilot-studies recently investigate and compare ABI patients' satisfaction and their performance (time and number of errors) in a Virtual Environment (VE) training using either a 2D or a 3D projection system. The preliminary results were very positive [26][27].

The literature indicates that, comparing to classical paper-and-pencil, and flat-screen computer rehabilitative tools, immersive VR systems prove capable of evoking a more intense and compelling sense of presence, thanks to the subject-environment interaction allowed (although it is also commonly associated to cyber sickness). However, much of the work in this area does not involve the use of fully immersive Head Mounted Displays (HMD). Studies reporting 3D projection screen and PC-based flatscreen approaches are providing useful information necessary for the reasoned development and implementation of VE technology [28].

THE CHALLENGE

In spite of some promising results, the lack of certainty regarding the advantages of applying this technology to a diversity of diagnostic situations, and the lack of methods, techniques, and tools for developing these types of programs require new studies in this area. Shortcomings of existing methods of cognitive rehabilitation, identified in scientific literature and in professional practice (such as patients' lack of motivation when confronted with exercises that repeat or that are distant from their reality), call for new rehabilitation programs.

This project's goal is to study the use of VR technology in the rehabilitation of executive dysfunction and memory, and the brain mechanisms involved. We focus on these processes because even patients who perform well on traditional neuropsychological tests for these specific cognitive abilities often display impairments in day-to-day activities, especially if the required competencies are part of the executive functions. Further, the complexity of this cognitive process makes assessment and rehabilitation through traditional psychometric and intervention methodologies questionable processes [29][30].

COMPUTER-ASSISTED REHABILITATION PROGRAM-VR (CARP-VR)

Our team is working in the development of a VR program, entitled CARP-VR. It consists of environments that simulate real life contexts in which patients will do various activities that are based on daily situations (e.g., shopping in a supermarket, navigating in city streets on foot or by employing a sequence of different means of transportation).

This project brings together a multiplicity of disciplines and a team of researchers and practitioners from different institutions (like Faculdade de Medicina da Universidade do Porto - FMUP, Instituto de Engenharia de Sistemas e Computadores do Porto – INESC/FE/UP, Centro de Reabilitação Profissional de Gaia - CRPG, Hospital de S. João – HSJ e Centro de Morfologia Experimental – CME/FM/UP), committed to contributing their expertise and experience to respond to this challenge. The project was recently submitted for a grant from Fundação para a Ciência e Tecnologia (FCT), in the domain of Investigation & Development Technology.

PLAN AND METHODS

Patients from two institutions (32 in each) will be selected to the project according to previously defined criteria decided by the project's team (e.g., time of injury onset, severity of the injury, time of hospitalization), ensuring that participants have capacity to handle the intervention tasks and potential for improvement and recovery. They will be divided into four intervention protocols: Patients receiving traditional cognitive rehabilitation, patients receiving no cognitive rehabilitation, patients under traditional cognitive rehabilitation receiving CARP-VR, and patients under no cognitive rehabilitation receiving CARP-VR. Each intervention protocol will have the duration of 6 months, the time we expect is necessary for improvement to occur.

The effects of each intervention protocol will be assessed through functional Magnetic Resonance Imaging (fMRI) and neuropsychological testing applied to participants and compared. Each group will be evaluated in the beginning and in the end of the interventions. Neuropsychological tests will include the *Frontal Assessment Battery* (FAB); *Behavioral Assessment of the Dysexecutive Syndrome* (BADS); *Wechsler Adult Intelligence Scale-III* (WAIS-III) – Portuguese version for special populations; *Wechsler Memory Scale-III* (WMS-III) – 1st Portuguese edition; *World Health Organization Quality of Life* (WHOQOL-BREF); *Goal Attainment Scale*; and *European Brain Injury Questionnaire* (EBIQ). The fMRI allows examination of brain mechanisms involved in the rehabilitation process, and neuropsychological tests allow the evaluation of cognitive functions, like EF or memory, for detection of gross cognitive deficits and for monitoring of improvement or decline in cognitive functions. Data from the neuropsychological tests will be analyzed using the *Statistical Package* for Social Sciences – *SPSS*; data from the fMRIs will be analyzed using Statistical Parametric Mapping through the *SPM Software Package*, which has been designed for the analysis of brain imaging data sequences.

It is expected that CARP-VR intervention will contribute to: Maintaining patients' interest in the task (namely via interaction through sensorial stimuli) and improving task performance, thus memory and EF (by providing the opportunity to develop specific and adequate interaction and problem-solving strategies), leading to cognitive gains. Additionally, it is expected that acquired capacities will be generalized to real-life activities and that results will remain three months after the end of the program, reflecting an amelioration of patients' functional independence and QOL.

Achievement of these results will constitute a great improvement in the area of cognitive rehabilitation, if patients become capable of actually transposing memory skills and other cognitive processes - employed and developed during program tasks - to the other domains of their lives, including functional, professional, and social.

Main Architecture of the VR Program

Because neurological patients may have mobility limitations, particularly if they are physically disabled, an interconnected system of training stations is being prepared to be located in different institutions. Two training stations will be developed and placed in two medical institutions located in the cities of Porto and Gaia.

The planned architecture of the training system is presented in figure 1. It includes the centralized back-office infra-structure that will allow remote synchronized updates and configuration of the training stations in the medical institutions. This centralized back-office will also keep up-to-date data on the results obtained by every participant in each training session. The therapist will then use these data to assess the state and evolution of each person with cognitive deficits and will prepare and assign the proposed training program accordingly.

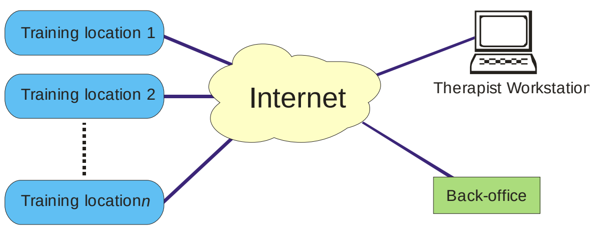

Figura 1 - Global architecture of the training system

All these analysis, preparation and configuration tasks can be performed remotely, from any computer with Internet access.

The centralized back-office runs on a single computer and includes a database server (MySQL) and an HTTP server (Apache). Communication between the centralized back-office and the training stations is performed in XML and transmitted using HTTP over the Internet.

Training Stations

Each training station will use a large screen and a stereoscopic projector to present visual training stimuli to the person with cognitive limitations. The image presented will be generated in a specialized computer with a stereoscopic graphics card. In order to allow stereoscopic vision, the trainee will use a set of shutter glasses, correctly synchronized with the generated images. The computer will also be used for generating sound stimuli, for receiving and interpreting the subject reactions and for communicating with the centralized back-office.

Human Machine Interfaces

Multimodal user interfaces allow person-computer interaction through different sensory channels than traditional interfaces [31]. Speech is the main sensory channel that humans naturally use to communicate with each other. It is natural, efficient, and flexible [32][33].

This work will include speech in addition to conventional interfaces (mouse, keyboard, and touchscreen). Speech recognition systems have undergone significant development in the last few decades. The reduction in word error rate, as well the decrease in recognition processing time, has resulted in more reliable systems [34]. This has brought these systems from the laboratory to user applications.

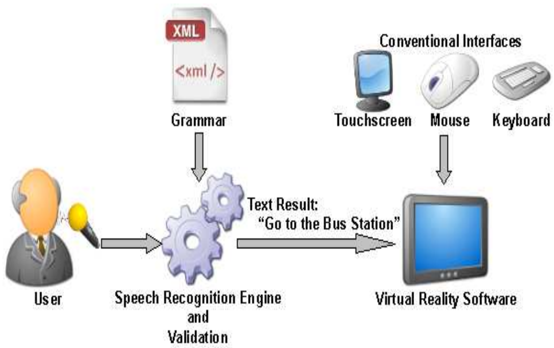

Figura 2 - Human machine interfaces

This interface allows people with cognitive and physical limitations to easily interact with the virtual reality software [35]. The speech recognizer in use is based on the Speech Application Programming Interface (SAPI) from Microsoft. This technology, which allows speech recognition in European Portuguese, was recently released by the Microsoft Language Development Center (MLDC). With this technology we can achieve a success rate in recognition of small sentences in the order of 90% [35][36], which is quite acceptable for this application.

CONCLUSION

We hope that this project will contribute towards the advancement of the scientific study of VR technology and its applications, and to improve our capacity to understand, assess, and treat the impairments typically found in TBI patients, especially in regards to memory and EF. With that we expect to contribute to patients' successful adjustment to real life situations and social reintegration.

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Artigo 5 - New Answers for Old Questions in the Domain of the Cognitive Rehabilitation

Dores, A. R., Carvalho, I. P., Guerreiro, S., Almeida, I., Romero, L., Abreu, C., Nunes, J. Leitão, M., Barbosa, J., & Castro-Caldas, A. (2009). *New answers for old questions in the domain of the cognitive rehabilitation*. Proceedings of "Interfaces and Human Computer Interaction 2009 and Game and Entertainment Technologies 2009". Algarve: IADIS, 91-96.

New Answers for Old Questions in the Domain of Cognitive Rehabilitation

Dores, A. R.[1], Carvalho, I. P.[2], Guerreiro, S.[3], Almeida, I.[3], Romero, L.[4], Abreu, C.[4], Nunes, J.[4], Leitão, M.[5], Barbosa, J.[6], & Castro-Caldas, A.[7]

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Abstract

This paper provides a brief introduction to rehabilitation in Portugal and presents some challenges posed by cognitive rehabilitation, especially in the case of acquired brain injury. Its purpose is to develop and investigate the effects of Virtual Reality in the rehabilitation of Disexecutive Syndrome. The authors describe the architecture of the VR Program under development and of a speech-enabled interface between patients and the program. Previous work analyzing patients' experience with this technology shows promising results, which makes the search for new solutions contributing to the improvement of effectiveness in this domain imperative.

Keywords: Executive functions, Cognitive rehabilitation, Virtual reality.

INTRODUCTION[11]

In the past few decades, Portugal registered very significant progress in policies and practices aimed at the disabled and handicapped (CRPG & ISCTE, 2007). With Portugal's integration in the European Community, funds targeted at this population became available and allowed professionalization of services that had been the responsibility of families until 1974.

Analysis of service user's profiles shows a universe of predominantly young males with congenital disabilities, especially in terms of mental, sensorial, and physical functions. However, the number of people acquiring disabilities due to accident or disease during their lifetime is growing. Traumatic brain injury (TBI) and stroke are particularly salient among the causes of acquired brain injury (ABI) in Portugal (Santos *et. al*., 2003; Castro, 2006; SPAVC, 2009). This population can be considered a paradigmatic case of the necessity of integrated services, still incipient in Portugal, as the consequences of brain injury can extend to all domains of human functioning: Physical, cognitive, behavioral, emotional, and social.

Of the cognitive limitations, dysfunction of executive functions (Disexecutive Syndrome) is particularly disabling. Difficulties in decision making, pragmatic communication, and high social inadequacy can become barriers difficult to overcome in social and professional (re)integration and in reacquisition of an independent life, pointing out the importance of rehabilitation. Thus professionals in this area frequently face the following dilemma: On the one hand, patients should have an active participation, and intervention should be developed in context; on the other, patients actually present a significant reduction in, or incapacity to interact with their environment.

From cognitive deficits to physical limitations and logistic issues such as lack of resources, a constellation of factors seems to render the desirable level of stimulation and the attainment of goals difficult. In the face of such difficulties, most rehabilitation programs happen in clinical contexts or in laboratory settings. However, according to Damásio (1994), there are four fundamental limitations to interventions in these contexts: Situations are not really present, but merely verbally described; decisions are only invoked, not performed; exercises fail in event sequencing (action-reaction); and action is temporally concentrated.

Existing services address physical rehabilitation. However, there is a shortage of multidisciplinary neuropsychological rehabilitation services targeted at the improvement of cognitive functioning, behavioral adjustment, and subsequent socio-professional reintegration of brain injury patients (DGS, 2003). Tailoring services to patients'

[11] As referências bibliográficas deste artigo encontram-se no formato proposto pela revista em que foi publicado.

experiences is a major challenge but a necessary goal. The development of an intervention plan which takes each patient into consideration individually requires the employment of a diversity of strategies and methodologies (Wilson, 1997). At the same time, the fact that neuropsychological rehabilitation is a clinical practice based on continuous and intensive training makes the promotion of motivation and of therapeutical adherence a priority. These can be seriously compromised due, for example, to patients' reduced awareness of deficits and of their impact (Prigatano, 1991; Prigatano & Fordyce, 1986).

Literature indicates that virtual reality (VR) can offer a promising response, given the limitations mentioned. It has been applied to the assessment and rehabilitation of several cognitive functions, such as executive function (EF), memory, spatial ability and attention, with positive results (see Rose *et al*., 2005, for a revision). Its application to EF started in the 90s, with the development of virtual environments (VEs) used in persons with TBI, multiple sclerosis and stroke. However, these environments were a version of a neuropsychological test – the Wisconsin Card Sorting Test (WCST) (Pugnetti *et al*., 1995, 1998). Today new environments are available, such as the V-Store, V-Tol, V-Wcst (see Castelnuovo *et al*., 2003, for a revision) or a virtual supermarket for people with mental insufficiency (Mello & Costa, 2005), also with positive results. But these projects' positive results do not convert them into finalized solutions, they constitute a stimulus for further development of new VEs. The diversity of abilities involved in EF, individual variety, and each country's specific reality require the development of research targeted at multiple and creative solutions.

By simulating situations and environments close to patients' experiences in real life contexts, VR increases the potential for generalization of the learned skills. It can provide specific environments that are appropriate for each patient, in conditions that are safe, and with a significant reduction in the number of professionals involved (Rose *et al*., 2005). At the same time, it can contribute to reduce performance anxiety associated with certain tasks and to increase patients' motivation and confidence in execution, leading to greater autonomy (Morganti, 2006). Grealy *et al.* (1999) further mention VR advantages in the rehabilitation of the capacity of planning, execution, and control, allowing the implementation of action sequences and complex behavioral patterns that daily life requires.

Despite these benefits, there are obstacles to the adoption of VR technology. In addition to being an area under (substantial) development in the domain of rehabilitation, it is also associated with the idea that it comes to replace therapists. It is urgent to demystify this idea, since VR can be viewed as an opportunity for developing tools that can help increase the success of interventions and be available to a greater number of patients. Another obstacle may result from the fact that patients and even therapists are not familiarized with this technology, which can generate some resistance. However, our practice has demonstrated that, when faced with pilot VEs developed by the authors, patients show great enthusiasm (Dores *et al*., 2007; Dores *et al*., 2008).

PLAN AND METHODS

The current work has the primary goal of studying the employment of VR technology in the area of EF rehabilitation in ABI patients. We will develop and implement VEs where subjects will solve daily life tasks, such as navigating in a city and employing different means of transportation, or shopping in a supermarket, with growing levels of complexity according to patients' performances. These VEs have several advantages over other programs: They are tailored to Portuguese reality and they consider and seek to address common limitations (as identified in clinical practice by therapists and other health professionals) patients face in their daily lives. The inclusion of a map editor in the final version is an additional advantage, permitting the alteration of the VEs according to intervention needs. The intervention modality in this VR program will include multimodal interaction with motor and speech commands, with the advantage of expanding the program utilization to a broader variety of patients. Still, the study of alternative forms of interaction is important for cases in which speech difficulties are also present.

Intervention effectiveness will be assessed by comparing results from VR implementation (VR Intervention Group, n=20) with those obtained in a traditional rehabilitation program (Traditional Intervention Group, n=20), and in the absence of intervention (Control Group, n=20), through neuropsychological tests and measures of quality of life. Each group will be evaluated in the beginning and end of the interventions. Neuropsychological tests will include the WCST; *Wechsler Adult Intelligence Scale-III* (WAIS-III) – Portuguese version for special populations; *Wechsler Memory Scale-III* (WMS-III) – 1st Portuguese edition; *World Health Organization Quality of Life* (WHOQOL-BREF); *Goal Attainment Scale*; and *European Brain Injury Questionnaire* (EBIQ).

It is expected that our intervention will contribute to: Maintaining patients' interest in the task (namely via interaction through sensorial stimuli) and improving task performance, thus EF (by providing the opportunity to develop specific and adequate interaction and problem-solving strategies), leading to cognitive gains. Additionally, it is expected that acquired capacities will be generalized to real-life activities and that results will remain after the end of the program, reflecting enhancement of patients' functional independence and quality of life. A follow-up study carried out three months after the end of the program is planned to assess these results.

2.1 Main Architecture of the VR Program

Because neurological patients may have mobility limitations, particularly if they are physically and/or cognitively disabled, an interconnected system of training stations is being prepared to be located, initially, at the CRPG, with the possibility to be placed in different medical institutions in the future, if it proves to be effective.

The planned architecture of the training system includes the centralized back-office infra-structure that will allow remote synchronized updates and configuration of the training stations in the medical institutions. This centralized back-office will also keep up-to-date data on the results obtained by every participant in each training session. The therapist will then use these data to assess the state and evolution of each person with cognitive deficits and will accordingly prepare and assign the proposed training program.

All the analysis, preparation and configuration tasks can be performed remotely, from any computer with Internet access. The therapist has continuous access to a map editor (figure 1) to define the environment configuration, namely streets, building locations, bus stops, etc. The map editor allows the possibility of having a set of configurations for several difficulty levels that can be applied according to the patient’s condition.

Figure 1 - Map Editor to specify the environment layout

2.1.1 Training Stations

Each training station will use a large screen and a stereoscopic projector to present visual training stimuli to the patients. The displayed image will be generated in a specialized computer with a stereoscopic graphics card. In order to allow stereoscopic vision, the trainee will use a set of shutter glasses, correctly synchronized with the generated images. The computer will also be used for generating sound stimuli, for receiving and interpreting patients’ reactions, and for communicating with the centralized back-office.

The VEs displayed to the patients are produced by specialized 3D modeling software. They are composed of buildings, vehicles, and building interiors, which include all the objects necessary for interacting with the environment, such as counters, cash registers, shelves, tables, etc. The aim is to mimic a real environment as closely as possible in such a way that a patient feels immersed within the world.

The application control component integrates and dictates all aspects of the interaction. It allows the user to choose a virtual environment, the interaction process, if necessary, and monitors the user's progress and the application's behavior. Is uses the Ogre 3D development environment to control the 3D world and all interactions associated with the VE (Junker, 2006). This open source graphics engine includes all the necessary controls for importing 3D object models and operating different kinds of interaction devices, usually associated with games.

2.2 Human Machine Interfaces

As mentioned before, the current project aims to offer a wide range of possible interaction means. Multimodal user interfaces allow person-computer interaction through different sensory channels (Oviantt, 2002). This is particularly important since patients' ability to deal with interaction devices may be limited. Devices such as keyboard, mouse or even joystick and touchscreen, commonly associated with a computer, cause several control difficulties to patients with motor disabilities, who are unable to operate, or even assimilate, the intricacies of these devices. Another natural, efficient, and flexible means of communication is voice (Privat *et al*., 2001; Yong *et al.*, 2002). Voice-like commands in VE allow people with cognitive and physical limitations to easily interact with the software, offering at the same time a path for adaptation to the real world. Speech recognition systems have become significantly more reliable due to reduction in word error rate, as well as decline in recognition processing time (Conn & McTear, 2000). Figure 2 shows the use of speech in addition to conventional interfaces.

The speech recognizer in use is based on the Speech Application Programming Interface (SAPI) from Microsoft. This technology, which allows speech recognition in European Portuguese, was recently released by the Microsoft Language Development Center (MLDC). With this technology, a success rate on the order of 90% can be achieved for recognition of small sentences (Abreu *et al*., 2007; Abreu, 2008), which is quite acceptable for this application.

Figure 2 - Human machine interfaces

Speech recognition systems transform acoustic speech signals into word sequences corresponding to commands that can be executed in the VR environment. The word sequences are analyzed and validated in order to determine if they correspond to a valid command. Based on sentence structure, analyses determine which Action, Quantity, Object, and Location are mentioned in the sentence (figure 3).

Action [ ] **Quantity** [ ] **Object** [ ] **Localization**

Figure 3 - Sentence structure

Action, Quantity, Object, and Location are keywords present (although not necessarily all four) in all the sentences. The square brackets (figure 3) represent optional connection words. The analysis considers that all the sentences are a potential command. The sentence is considered a valid command if one of the commands stored in the Valid Commands Database contains the same keywords as the sentence under analysis. To verify if the sentence is a valid command, a vector is created that contains all the keywords of the sentence under analysis. If it is possible to create another vector with the information from the database, and $\vec{V}_{RecognizedSentence}(A,Q,O,L)=\vec{V}_{Database}(A,Q,O,L)$, where A is Action, Q is Quantity, O is Object and L is Location, then the sentence is considered a valid command and the respective information is sent to the virtual reality environment software.

CONCLUSION

The development of innovative tools and technologies, such as VR, and the study of their effects in a variety of diagnostic situations are urgent, especially in ABI patients. A multidisciplinary approach to this endeavor, involving professionals from different areas, will ensure an intervention that both fits the current economic juncture of contention and optimization of resources, and can play a crucial role in adapting services to citizens' needs, maximizing their access to rehabilitation and to professional formation, and their return or access to employment, in many cases a necessary condition for resuming life.

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Artigo 6 - Computer-Assisted Rehabilitation Program – Virtual Reality (CARP-VR): A Program for Cognitive Rehabilitation of Executive Dysfunction

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Computer-Assisted Rehabilitation Program – Virtual Reality (CARP-VR): A Program for Cognitive Rehabilitation of Executive Dysfunction

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Abstract

Every year millions of individuals sustain Acquired Brain Injury (ABI) often resulting in physical, cognitive and psychosocial deficits, leading to life-long changes in the quality of life of patients and their families. In the domain of rehabilitation, virtual-reality (VR) technology has assumed a crucial role in the creation of innovative assessment and training programs. The purpose of this study is to present the Computer-Assisted Rehabilitation Program (CARP-VR) after a brief review of the state of the art. CARP-VR was tailored to the rehabilitation of executive functioning and other related cognitive functions in patients with ABI. It consists of virtual environments that simulate real-life contexts in which patients perform various activities that are based on daily situations. The final version of CARP-VR is now ready to be employed, and tests have been designed to validate it as a tool for the rehabilitation of executive functioning and related cognitive functions.

Keywords: Virtual Reality, Cognitive Rehabilitation, Executive Dysfunction.

1 The Neuropsychology of Executive Functions: From Cognitive Assessment to Cognitive Rehabilitation[12]

Neuropsychology can be defined as the field of knowledge dedicated to the study of the neural mechanisms in its relations to cognitive functions and behavior. It is thus a field of neurosciences that involves cognitive sciences, behavior sciences and their interception [1].

In terms of pathological conditions, neuropsychology seeks the treatment of cognitive and behavior deficits resulting from changes in the functioning of the Central Nervous System (CNS). These dysfunctions may stem from an abnormal development of the nervous system or be acquired throughout the course of life. Regarding acquired injuries, neuropsychology has been confronted with new and demanding challenges resulting from life in modern societies. We are referring here to Acquired Brain Injury (ABI) resulting from Traumatic Brain Injury (TBI) or from neurological diseases, such as stroke. Traffic accidents or work-related accidents are frequently in the origin of TBIs, and a sedentary style of life is, among other causes, in the origin of stroke.

The considerable scientific, social and political advances of the last decades in developed countries have contributed to the development, in this area, of innovative prevention, acute-phase care and rehabilitation services. Despite these efforts, young, active adults continue to face the impossibility of providing continuity to their life projects, temporarily or permanently, as a result of ABI.

Among multiple cognitive deficits, such as those that affect visuospacial functions, attention or memory, we highlight the ones affecting executive functions (EF) for being particularly disabling. Dysfunction at the level of EF is usually called executive dysfunction or dysexecutive syndrome. Associated with the pre-frontal cortex, it appears, more than any other cognitive process, to determine the extension of patient recovery because, in case of dysfunction, all other systems may indirectly be affected [2].

Executive functioning is therefore a complex cognitive process that encompasses other cognitive processes. It refers to the cognitive capacities involved in behavior initiation, planning, sequencing, organization and regulation [3]. In addition to typically failing in the elaboration of the action plan, patients also have impulsive actions and difficulties in mental flexibility [4]. As a consequence, they display great limitations in daily-life activities.

Given the negative impact that executive dysfunction has in the life of patients and their families, it is surprising that only in recent years has it assumed a prominent place in the literature. Several factors may be in the origin of this delay, namely, the inexistence of

[12] As referências bibliográficas deste artigo encontram-se no formato proposto pela revista em que foi publicado.

clearly effective rehabilitation programs, the lack of theoretical consistency concerning the nature of EF, the diversity of deficits associated with it and the limited consciousness patients have concerning their deficits and the impact these have in their performances [5]. The limited ecological validity of neuropsychological tests targeting EF adds to these difficulties [6].

With respect to cognitive rehabilitation as a basic component of neuropsychological rehabilitation, an increasing number of reviews and scientific papers have suggested that it can bring significant benefits and give the quality of life back to patients and their relatives [7]. However, specific results of EF rehabilitation strategies, as evidence of its effects, even though gradually increasing, remain limited [8]. In spite of this, some strategies, such as problem-solving training and its application to people with TBI, or cognitive interventions that promote internalization and self-regulation strategies through self-monitoring and self-instruction have positive effects [9].

The development of new methods and EF rehabilitation tools grounded both in theory and in clinical practice, whose prescription can be based on ecological assessment, is a current requirement and the central subject of the work we propose. It will constitute a major contribution for research and for practice in this area [10].

2 The Advantages of VR in the Assessment and Rehabilitation of Executive Dysfunction

The above circumstances justify the inclusion of innovative technologies in the process of assessment and rehabilitation that may help to overcome some of the main limitations of current interventions. The democratization of information and communication technologies (ICT) made it possible for Virtual Reality (VR) to stop being a privilege of certain areas, such as the cinematographic industry, and be at the service of rehabilitation.

VR has been defined as “an advanced form of human-computer interface that allows the user to ‘interact’ with and become ‘immersed’ in a computer-generated environment in a naturalist fashion” [11]. “Sensory data generated by a computer system may be perceived as physical reality, especially when perception is enabled by use of the body in a manner similar to physical reality. The system ideally displays in all sensory modalities; fully encloses the person in these displays; tracks head position and orientation but also the movements of the whole body, determining the visual stereo and spatialised auditory displays as a function of this tracking” [12].

Three distinctive characteristics of VR are: presence, involvement and interaction. The first one refers to “the illusion of being in the rendered virtual place. When contingent events in the virtual world apparently relate directly to the participant, then further there is the illusion that what is occurring is real. Under these conditions participants tend to act and respond to the virtual reality as if it were real" [12]. Involvement can be defined as participation/persistence of the users in the task, or as their motivational degree. Finally, interaction is the capacity of the virtual environment (VE) to react to the user's action; the more the immediate environment changes in response to this action, the more interactive the VE is.

Thus this technology allows the creation of stimuli with identical properties to real ones. Its mere three-dimensionality confers an increased sensation of presence to the user, making laboratorial emulation of the reality possible. In fact, computer-generated VEs are more and more realistic.

The development of VR technology has increased considerably, with application in areas such as engineering, defense, medicine, education, entertainment, art, design, and visualization [13]. VR has also been successfully applied to some clinical domains in mental health, such as phobias, post-traumatic stress disorder, post-traumatic stress associated with traumatic brain accident, addictive behavior and other impulse disorders, panic disorder, eating disorders, disorders of the autism spectrum, cerebral palsy, attention deficit hyperactivity disorder, or even to increase the level of independence of the elderly. A review article also shows the effects of its use in people with intellectual incapacities, including in the promotion of important abilities for independent life, indicating that, with the exception of autism spectrum disorders, the distrust regarding transference of acquired competencies into real-life was unfounded [14].

More recently, VR technology has been applied to neuropsychological assessment and rehabilitation. Even though its applicability to this area was identified more than ten years ago [13], it seems to have attracted particular interest recently [15-20], including in Portugal [21-24]. Among the advantages of using VEs in cognitive assessment and rehabilitation, as well as in research, are the stimuli of easy manipulation and higher ecological validity inasmuch as they are more realistic than traditional stimuli.

Advantages of VR which make it possible to overcome the limitations of neuropsychological assessment through the traditional methods are: (1) the provision of real-world distractions and stressors; (2) increased interactivity and immersion; (3) enhanced flexibility and capacity for self-initiation and structuring of behavior; (4) better reliability and control; and (5) improved patient compliance and motivation [25]. Although these characteristics have been, until now, less explored in terms of rehabilitation, the advantages they brought to assessment are also applicable to the latter domain. Many authors have described the benefits that VR can bring to evaluation/rehabilitation, namely a more naturalistic or "real-life" environment, control of stimulus presentation and response measurement, safe assessment of hazardous situations, increased generalization of learning, increased standardization of rehabilitation protocols, and increased user participation [11].

Different cognitive functions, such as attention [20], memory [26], spatial transformation/reasoning [27], and executive functioning [6] have benefited from VR applications. A literature review concerning the use of VR in the assessment and rehabilitation of different cognitive processes such as spatial capacity and visual perception, attention, memory and executive functioning signals this technology's potential [4].

VR can bring additional benefits to rehabilitation, including the possibility of patients performing exercises at a distance, in the comfort and safety of their homes. Many patients still do not have immediate response from health services, remaining on waiting lists. Others can not benefit from therapy because of moving difficulties between their houses and health services. In these cases, VR may be the only possible solution. Additionally, it may allow the continuation of the rehabilitation program after patients are released. It operates as a networked and virtual organization, of which patients and therapists are part, with the goal of rehabilitation. Thus, VR does not come to replace the therapist. In the situations presented, monitoring the progression of the patient is essential, even if not presencial, for program planning, analysis and discussion of results. It is also desirable that such programs are integrated with other interventions, in order to provide a holistic approach to the patient.

The main difficulties for a generalized use of VR training in rehabilitation are still the selection of the adequate interaction devices and methods. The interaction methods must allow the navigation in detailed 3D environments and the manipulation of specific objects, always providing feedback information to the patient. This must be achieved in a way that can be considered natural and intuitive for several different users with diverse disabilities, backgrounds and practices. Even with the large diversity of available interaction gadgets (joysticks, mouse, gloves, trackers, etc.) and feedback media (image, sound, tactile stimuli), there is not a perfect solution that fits all the requirements and that can be considered easy to use and intuitive for all individuals with disabilities. Due to these difficulties, a usability test is being performed, addressing several different interaction solutions. This experimental work is described in section 5 and should be detailed in a forthcoming publication.

3 Computer-Assisted Rehabilitation Program – Virtual Reality (CARP-VR)

The current work has the main goal of studying the application of VR technology specifically in the area of rehabilitation of EF, but also in other cognitive functions such as visuospatial functions, attention and memory, in patients with ABI. CARP-VR consists of

VEs that simulate real-life contexts (e.g., a house and a market) in which patients perform various activities that are based on daily situations (e.g., shopping). The tasks included in each activity have growing levels of complexity according to patients' performances.

3.1 The Development Process

The development of CARP-VR was based on the systematic review of scientific literature, expert consultation and the incorporation of changes resulting from refinement of the process itself. Our development process incorporates Sohlberg and Mateer's (1989) Model [2], specifications in the domain of rehabilitation, and considers the work of authors in the field of VR technology and serious games [28-29]. A detailed description of this proposal can be found in Dores, Carvalho and Castro Caldas (2009) [10]. For the first task, Theoretical Review and Practical Reflection, the Mateer (1999), Sohlberg and Geyer's (1986), and Ylvisaker's (1998) works provide theoretical support for the task of EF rehabilitation [30-32].

3.2 General Features

CARP-VR consists of two distinct environments. The first one, called Training Environment, is a house. The second one, the rehabilitation VE proper, is a car parking lot and a supermarket.

In the Training Environment, the patients can explore three different scenarios: Scenario 1 - storage room; Scenario 2 - dining room; Scenario 3 - bedroom.

In these scenarios the subjects need to solve different tasks of increasing complexity but low level of demand, because it is a training environment. The skills required are: recognition, sorting and problem solving, respectively.

In terms of the development process, the Training Environment aims to: (1) help decide the VE design, the hardware, the software and the visualization system to be used in the complete CARP-VR; (2) assess the degree of user satisfaction with it, first with healthy participants, then with ABI patients. In terms of its later use (as already part of the final CARP-VR), the Training Environment aims to allow patients to experience the VR technology and train navigation before beginning the rehabilitation program itself.

The structure of the Rehabilitation Environment consists of two phases: an assessment phase and a rehabilitation phase. The assessment phase will not be detailed here since it is the accomplishment of each rehabilitation task at the intermediate level. In addition to the rehabilitation task of each of the cognitive functions, we create different levels that are associated with them. These levels stem from the variation of a set of parameters that we now describe: Products' list (visible or not); List format (Auditory or Visual); Instructions (Yes/No - Y/N); Delayed start (Y/N); Repetition (Y/N); Error allowed

(Y/N); Corrections (Y/N); Number of items to be purchased; Number of sections; Products' prices (Y/N); Supermarket map display (Y/N); Alarm (Y/N); Magic words – for the training of self-instruction, according to the *Goal Management Training* [33]; Time limit (Y/N); Temporal assessment; and Special Requirements (involving problem solving). These are articulated as to increase the difficulty of the tasks throughout the program.

4 System Architecture and Technical Specifications

CARP-VR is a real-time simulation of a supermarket in which patients can perform the tasks that they would normally do in such an environment. The simulation is powered by a real-time game engine, which grants an experience level similar to what is expected in a computer video game. This allows patients to fully interact freely with the objects in the supermarket, without any pre-computed paths or pre-established tasks.

The first version of the simulator was developed in C++ and used OGRE as the graphics engine. OGRE is "one of the most popular open-source graphics rendering engines, and has been used in a large number of production projects, in such diverse areas as games, simulators, educational software, interactive art, scientific visualization, and others" [34].

This graphics engine was chosen due to its recognized performance and because the available higher-level simulation engines, like NeoAxis Engine, version 0.9, NeoAxis Group, were not considered mature enough at the beginning of this project [35].

Later, the requirements for rapid preparation of several different simulation environments justified the evolution to a second version of the simulator. This new version was implemented in C# in order to take advantage of the NeoAxis Engine. NeoAxis is a proprietary game engine, free for non-commercial use that offers a fully integrated development environment for interactive simulation applications [35]. The use of the map editor, the object editor and other NeoAxis Engine high-level functionalities allowed a faster and more intuitive implementation of the required training environments [35].

4.1 Maps and Levels

All elements in the map, from shelves to individual products, were modeled in Autodesk Maya 2011, version 12.0, Autodesk, and then exported to the Ogre 3D format [36]. Once made available in the NeoAxis map editor, the different elements can be put in place according to their type. Shelves and other stationary elements are made static, to improve rendering, while products are assigned to a special interactive object.

In addition to objects, each map has a number of areas which allow the simulation to "know" if the patient visited those sections inside the supermarket. Also, special areas can be defined that allow a patient to perform specific tasks, like taking a ticket for the line in the meat section.

Once everything is in place — shelves, products and areas — the user can start to create levels. The levels are created in a special editor strictly designed for this purpose. Not only can the levels be edited, but the product and the areas can also be defined, and their properties, like price and category, can be assigned.

Each level is made of a number of tasks that the patient has to perform and complete successfully in order to progress in his/her rehabilitation.

These tasks were carefully crafted as the basic rules upon which all levels can be created. Beyond the most straightforward tasks that can be performed in a supermarket (e.g., select a product from a shelf and proceed to payment), other simpler rules were created to help patients in their rehabilitation process. These rules include the availability of aiding information, like the mini-map, the shopping list and the magic words, the amount of time available to complete all tasks, which includes the collection of the products and their payment, the amount of available money, which can be exact — according to the shopping list —, below or above needed, the areas that the user must visit and, of course, the shopping list. Also, the quantity of products to be acquired can be expressed. Each level has a textual description, shown to the patient upon level start, which contains the tasks that must be performed on that level. Also, an audio file can be supplied at each level, which will be played at the beginning of the level, providing this way an auditory description of the tasks at hand. Other auditory cues are available in the rehabilitation programme, like the right/wrong sound, or a sound stating that the patient chose a product not on the list.

In a more technical view, this editor was created with Windows Forms, API included in the .NET Framework, Microsoft [37] and data serialized using the facilities provided by the .NET Framework, version 4.0, Microsoft, 2010 [38].

4.2 Simulation

The simulation starts by asking the name of the patient and whether he should start from the previous level – the level where he was during the previous session – or from the beginning. This is the only area in the simulation designed to be accessed by the therapist. Thus, it is the only one that is based on a mouse model. From this point on, all interactions are based on joystick.

This interaction model was used in order to overcome the difficulties presented by patients, who, by the nature of their condition, are prone to co-ordination problems. The cart moves with joystick by moving its principal axes. By rotating the handle, the patient can look up and down. The same button is used for almost all actions: dialog box interaction — when a message box is shown —, and acquire a product. The help buttons, map, shopping list, return item to the shelf, are mapped to keys in the joystick so that the patient does not have to wonder with a cursor on the screen.

All acquired products are visible inside the cart, so the patient does not have to remember which products have already been bought. If the shopping list is available, any acquired product on the list will disappear from it, indicating that the product has been bought. Products not on the list can be either put in the cart or not, depending on the settings of each level.

Also, depending on the level settings, the user can put products back, by means of a dialog box, also controlled by joystick.

The simulation either ends once all products on the list have been bought, or once the patient reaches the payment area. In this case he has to successfully pay for the products in the cart. This is also determined by the level settings. A successful payment depends on getting all products from the shopping list and on the amount of money the patient has available.

If he/she has enough money, he must pay in cash. Otherwise, he can pay by credit card. Once the patient gets to the payment area, a dialog box appears with all the items he has in the cart, along with the cost of each one and the amount purchased, like in a real supermarket.

If the patient successfully completes the level, a new simulation will be presented with extra difficulty. In case of failure, the patient either repeats the level a number of times until he gets it done, or the difficulty level is lowered, depending on the settings of the map.

4.3 Storing information

For each patient, at the very beginning of the treatment, biographic data are collected and stored in a MySQL database, MySQL Community Edition, version 5.5.11, available on site or remotely – for a more centralised management of the patients [39]. A separated application was developed in Java to manage patients' data, allowing the therapist to analyse the patient's biographic data and performance independently from the CARP-VR player or editor. In a near future, the CARP-VR player will store the performance data on the same database, associating each patient with his/her own statistical data, and will receive the last played level, allowing the patient to resume the therapy session -- at present, this feature is only available locally, in each computer where the CAPR-VR player is available. Once the CARP-VR player is able to upload data to the MySQL database, the independent Java application can be extended to show each patient's evolution graphically.

5 Usability Testing

Usability can be defined as "the extent to which a product can be used by specified users to achieve specified goals with effectiveness, efficiency and satisfaction in a specified context of use" [40]. Users' satisfaction in interacting with the product and this latter's utility have become crucial in today's software conception and development. Despite still quite often neglected, analysis of product usability can facilitate future users' acceptance of the application, performance and satisfaction [41-42]. We also consider users' motivation. Exploratory testing and evaluation, performed during program design and developmental stages by the development team and by healthy subjects allowed us to consolidate the functioning of the system, but do not necessarily ensure its adequacy to future users' real needs [43]. Thus we have conducted tests specifically with the population that CARP-VR targets. In this case, the different VEs developed have been independently tested in pilot studies, and results are presented elsewhere, as they are out of the scope of this paper. Results are promising, supporting the usability of the VR program and showing its relevance in subjects' motivation to participate in the rehabilitation process, which also reflects their satisfaction with it. They are presented in detail elsewhere, as they are out of the scope of this paper.

6 Ongoing Developments and Conclusion

Ongoing tests are designed to contribute to validate CARP-VR as a tool for the rehabilitation of EF and related cognitive functions. Results from pilot-studies contribute to the final version of the program in terms of its usability and subjects' motivation and satisfaction with it. The test of the final prototype is currently in progress with healthy subjects and subjects with pathology. The two groups will be compared and the overall results correlated with those obtained in traditional neuropsychological tests. In future work we expect to test the generalization of acquired skills to real-life tasks and the maintenance of acquired skills in follow-up studies. Hopefully, this work will enable clinicians to take advantage from VR technologies in the field of neuropsychological rehabilitation.

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Artigo 7 - Serious Games: Are They Part of the Solution in the Domain of Cognitive Rehabilitation

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Serious Games: Are They Part of the Solution in the Domain of Cognitive Rehabilitation?

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Abstract

Serious Games are in increasing use for serious purposes, such as health. Particularly in the field of cognitive rehabilitation, they can offer new solutions that are fun, user-friendly and goal-directed. In this study, a prototype rehabilitation platform is presented, aimed at intervening in executive functioning and other related cognitive functions in patients with Acquired Brain Injury. It was tested in three studies investigating patients' satisfaction and performance in a virtual environment using 2D computer-screen or 3D projection-screen approaches, and patients' satisfaction with the virtual reality (VR) program regarding its usability and role in motivation to participate in the rehabilitation process. Contributing to the final version of the program, results in our pilot-studies are promising, supporting the usability of the VR program and showing its relevance in subjects' motivation to participate in the rehabilitation process.

Keywords: Serious Games, Virtual Reality, Health Care, Cognitive Rehabilitation, Executive Dysfunction.

1 Introduction[13]

Today we are witnessing social changes in perceptions and attitudes regarding deficiency and disability. These changes reflect a transposition of handicap conditions from the individual sphere, to which they were traditionally confined, to the public domain. Today's greater visibility of these phenomena, the professionalization of the services directed at them and the increase in demand for such services make the need for innovative practices even more pressing [1]. It is crucial that these practices promote equity in the access to the services, the success of interventions and the understanding of the mechanisms underlying intervention effects. The development of game design and technologies, as well as other technologies, like Virtual Reality (VR), has contributed to these purposes [2, 3, 4, 5]. For a long time, these resources were applied almost exclusively to domains such as the movie industry and games. Their main purposes were enjoyment, fun and entertainment [2]. With the democratization of their use, other areas can now benefit from their potential, particularly Health Care.

In this paper we discuss the possibility of using so-called Serious Games (SG) in the field of health, especially in rehabilitation. We introduce the Computer-Assisted Rehabilitation Program – Virtual Reality (CARP-VR) developed as an instance of SG tailored to the rehabilitation of executive functioning (EF) and other related cognitive functions in patients with Acquired Brain Injury (ABI). Finally, we present the preliminary testing of CARP-VR in three studies with ABI patients investigating patients' satisfaction and performance in a VE using two-dimensional (2D) computer-screen or three-dimensional (3D) (eyeglasses) projection-screen approaches, and patients' satisfaction with the VR program regarding its usability and role in motivation to participate in the rehabilitation process.

2 Serious Games: Is what is beautiful, good?

SG can be defined as "a mental contest, played with a computer in accordance with specific rules, which uses entertainment to further government or corporate training, education, health, public policy, and strategic communication objectives" [6]. They are "games that engage the user, and contribute to the achievement of a defined purpose other than pure entertainment (whether or not the user is consciously aware of it)" [7]. Their characteristics and applicability to distinct areas led to an exponential growth of SG in the last decade [7].

In the domain of health we highlight their application to motor rehabilitation, including balance, upper limbs or wheelchair mobility, and cognitive rehabilitation, as in spatial

[13] As referências bibliográficas deste artigo encontram-se no formato proposto pela revista em que foi publicado.

capacity, visual perception, attention, memory or executive function. In this work we will focus on the field of cognitive rehabilitation [8, 9, 10, 11, 12].

Cognitive rehabilitation, as part of neuropsychological rehabilitation, can improve competences or minimize deficits. It refers to the "(…) therapeutic process of increasing or improving an individual's capacity to process and use incoming information so as to allow increased functioning in everyday life." [13].

Cognitive rehabilitation can have the goal of intervening on: (1) disability, seeking to stimulate and improve altered functions by direct action on these functions (restoration), (2) promoting the use of alternative mechanisms or of preserved skills (compensation), or (3) using different strategies to help minimize problems resulting from the dysfunction (replacement) [14].

When functionality and problem-solving abilities are significantly impaired due to dysfunction at the level of memory and executive functions (EF), cognitive rehabilitation becomes particularly important. EF refers to cognitive capacities involved in initiating, planning, sequencing, organizing, and regulating behavior [15], indispensable to the most basic tasks of daily life such as independent mobility or supermarket shopping. In fact, at the cognitive level, impaired memory and executive dysfunction are two of the most pervasive and disabling consequences of brain damage [16, 17, 18, 19, 20].

SG may allow goal-directed exercises, performance monitoring, immediate feedback and customization. The environment, level of difficulty and speed of progression are part of the parameters that can be dynamically adapted to the real needs of each subject, their abilities and performance [7, 10]. Also, SG are compatible with other technologies, like VR, with its characteristics of presence, involvement and interaction [6, 9, 21]. These are important advantages of SG over traditional rehabilitation tools. The already mentioned potential of SG in different areas has stimulated the creation of multidisciplinary teams involved in the design, development, testing and implementation of rehabilitation programs. However, the balance between "science", "engineering" and "entertainment" or, in other words, between "engineers", "artists" and "scientists" is complex. Their diverse backgrounds provide them with different perspectives on the process [22]. This can be a difficulty – for example, if too much importance is placed on technology in detriment of the ends towards which it is intended – or an asset, with collaboration giving rise to new questions and solutions on old problems. Authors such as Bermùdez i Badia showed the importance of answering the question of what matters most, whether to improve the way therapy is made available or its working principles[22]. Very sophisticated and technologically advanced interventions do not always mean better interventions. The opposite also seems true.

In the field of rehabilitation, the motivation that gaming factors provide is a crucial dimension, as rehabilitation is a long, repetitive, dull and intense process, with often slow progress and, in some cases, personal unawareness of deficits [23]. However, the design of more effective rehabilitation tools cannot fall exclusively on the promotion of motivation. Theoretically supported designs of exercises / tasks for innovative rehabilitation of different cognitive functions are also crucial. Additionally, it is important to understand the mechanisms underlying recovery, for example in the case of restoration [24].

Reconciliation of these multiple objectives will certainly be part of all interventions in the future, which can bring significant progress to rehabilitation in the years to come. This progress is also due, in part, to the rapid evolution that other areas, like the field of neuroimaging, have also undergone [25, 26]. These considerations highlight the importance of strong principles guiding the process of developing any intervention/rehabilitation tool. Among them, evaluation should be considered a requirement crucial to the process, not a superfluous dimension [27]. Also important is the involvement, since the program's conception, of those for whom it is intended [28, 29]. Only this way can such technologies', and each specific program's effectiveness and efficiency in rehabilitating be ensured, and satisfaction with their use granted [30].

3 Our Contribution: Attempting to take part of the solution

Our team is working on the design, development and implementation of CARP-VR (Computer Assisted Rehabilitation Program-Virtual Reality). The CARP-VR rehabilitation system is an interactive virtual environment simulator of real-life contexts in which patients perform various activities that are based on daily situations. Rehabilitation sessions are composed from a sequence of levels that the patient has to complete successfully in order to progress to the next level. The success in a level depends on the fulfilment of a predefined list of tasks.

3.1 CARP-VR Architecture

The CARP-VR rehabilitation system is built into two distinct applications (Fig. 1): the CARP-VR Editor is the back-office interface, where the therapist defines the simulation environment and required tasks for each level. This therapist's working station also includes the results manager to allow the study of individual performance in the training sessions. The CARP-VR Player is the interactive virtual environment navigator. It allows the patient to train the execution of the specified task events and registers all actions and progress in the system's database.

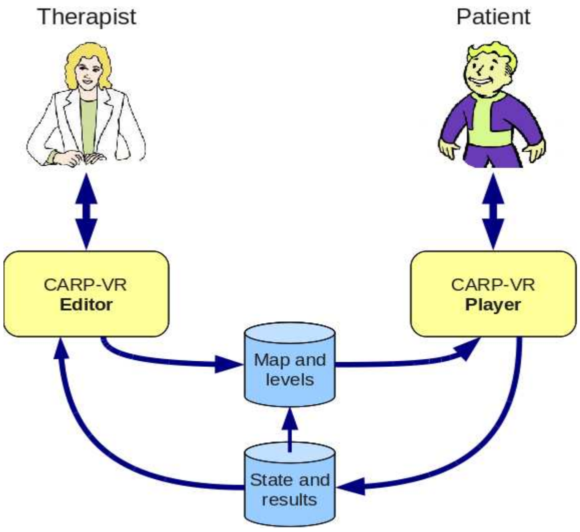

Fig. 1 - The CARP-VR Rehabilitation System

3.2 CARP-VR Player

The Player is the CARP-VR rehabilitation system's main application. It is built in the C# programming language and uses the NeoAxis Game Engine for the simulation and visualization of the 3D virtual environments [32]. NeoAxis is a proprietary game engine, free for non-commercial use, that offers a fully integrated development environment for interactive simulation applications. NeoAxis was developed over the OGRE graphics engine, which is one of the most popular and complete open-source graphics rendering engines [33]. The functionalities delivered by the OGRE graphics engine allow the use of a wide set of geometric formats and visualization and iteration devices in the developed CARP-VR player [33]. The functionalities provided by the NeoAxis games engine provided a physically-based simulation of the virtual objects and a more direct specification of the desired rehabilitation events [32].

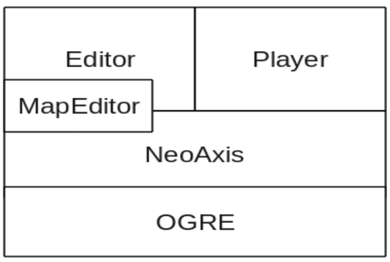

Fig. 2 - The development stack for the CARP-VR Editor and Player

3.3 CARP-VR Editor

The CARP-VR Editor is the set of tools used by the therapist. It is used to prepare and test the rehabilitation sessions before they take place, to monitor patients' behaviour in real time during the rehabilitation sessions and to access and analyse the results registered after each rehabilitation session. Like the CARP-VR Player, this Editor uses the NeoAxis game engine, version 0.9, from the NeoAxis Group„ but it also takes advantage of the NeoAxis map editor [32]. This extra module, included in the NeoAxis integrated development environment, allows a fast and friendly preparation of the different required simulation scenarios and levels [32].

Rehabilitation session results are accessed from the therapist's working station using some database interface modules, developed using the .Net framework and the SQL queering language. For each patient, results can be obtained in either an accumulated way or for each independent rehabilitation session.

3.4 Database

The CARP-VR rehabilitation system's database stores the definition for the simulated environments, the behaviour of movable simulated entities, the guidelines for the rehabilitation sessions, the state of rehabilitation and specific data for each participant, and the results produced in each realised rehabilitation session. As figure 2 shows, this database is organized in two different sets.

All the virtual environments used in rehabilitation are described in typical 3D scene files, in the native Ogre3D or in any other format supported by the OGRE graphics engine. All the data related to each patient and the results from each rehabilitation session are stored in a relational database, implemented by a MySQL database management system [34].

Due to the high number of different required rehabilitation environments and levels, the rehabilitation environments can be completed and adjusted for each level in real time, according to multiple level specifications also stored in this relational database.

3.5 Rehabilitation environments

A virtual environment of a home has been developed and has been employed as a training and assessment environment, used by every patient before starting the rehabilitation program. It aims to prepare patients to use the VR Program itself, including how to navigate in the virtual environment and the kind of tasks that can be performed there. In the Training Environment, the patients can explore three different scenarios: Scenario 1: storage room; Scenario 2: kitchen (Fig. 3a); Scenario 3: bedroom. In these scenarios the subjects need to solve different tasks of increasing complexity but low level of demand, because it is a training environment. The skills required are: recognition (to select the products asked for), sorting (to select the products asked for in a specified order) and problem solving (to select the products asked for in order to perform a certain task), respectively.

(*a*) (*b*)

Fig. 3 - The Training Environment (a) and the Supermarket (b)

Results presented in this paper were produced using this training environment and the rehabilitation environment of a typical supermarket and the surrounding parking lot (Fig. 3b). The tasks included in this environment have growing levels of complexity and demand according to patient's performances, and the program's gaming components include the growing number of sections to visit, products to acquire, and problems to solve. Parameters that can change, generating the different levels, are: Products' list (visible or not); List format (Auditory or Visual); Instructions (Yes/No - Y/N); Delayed start (Y/N); Repetition (Y/N); Error allowed (Y/N); Corrections (Y/N); Number of items to be purchased; Number of sections; Products' prices (Y/N); Supermarket map display (Y/N); Alarm (Y/N); Magic words – for the training of self-instruction, according to the Goal Management Training [18]; Time limit (Y/N); Temporal assessment; and Special Requirements (involving problem solving). These are articulated as to increase the difficulty of the tasks throughout the program [31]. Other rehabilitation environments (e.g., a citizen shop) are under development for future use.

4 Usability Testing

Usability can be defined as "the extent to which a product can be used by specified users to achieve specified goals with effectiveness, efficiency and satisfaction in a specified context of use" [30]. Usability, an essential condition for the acceptance of the product by the user, should be tested throughout the development process, even during the interface design [28, 29]. Thus we conducted tests with the population that CARP-VR targets. The results (presented in study 3, below, for ABI patients), as well as those obtained in the new tests that are in course, are considered and integrated (in terms of environments and exercises) in the program under development.

4.1 Study 1

Goal. To test the usability of the Training Environment (see section 3, above), in the 2D visualization mode [6, 7].

Participants. Eight subjects with ABI, 6 males (75.0%) and 2 females (25.0%), mean age of 30.5 years old (SD=7.4), mean education of 10 years (SD=4.0), were recruited.

Procedure. We tested the time spent in the tasks in each scenario (Scenario 1: storage room - recognition; Scenario 2: kitchen - sorting; Scenario 3: bedroom - problem solving. Two evaluations were conducted four days apart (Test 1 vs Test 2). The virtual environments were visualized in a 2D computer screen.

Results and Discussion. We observed improvements in all participants within the time needed (on average) to perform the requested tasks. From the first to a second test, time reduction varied between 27% and 75%. The number of errors decreased as well. The study also shows the potential of VR technology in terms of subjects' motivation for the task. We observed a strong involvement in carrying out tasks. An after-task questionnaire survey further displayed the patients' desire to continue that kind of tasks.

Table 1 -Time participants (P1 to P8) spent in the tasks by scenario

	Scenario 1		Scenario 2		Scenario 3				
	Test 1 (min)	Test 2 (min)	Test 1 (min)	Test 2 (min)	Test 1 (min)	Test 2 (min)	M Test 1	M Test 2	Time improvement
P1	6.53	1.57	5.35	0.47	1.23	1.22	4.37	1.09	75%
P2	1.24	2.54	5.14	0.40	3.22	2.21	3.20	1.72	46%
P3	6.00	2.54	17.30	5.05	7.00	2.06	10.10	3.47	66%
P4	2.19	1.15	3.40	1.26	1.57	1.14	2.39	1.18	51%
P5	1.33	0.38	0.49	1.14	2.10	0.44	1.31	0.65	50%
P6	7.45	2.40	4.44	5.26	3.32	2.40	5.07	3.35	34%
P7	3.38	4.55	3.20	4.31	7.00	1.33	4.68	3.40	27%
P8	1.26	0.50	1.05	0.55	0.33	0.37	0.88	0.47	47%

4.2 Study 2

Goal. To compare subjects' performances and satisfaction with the same training environment of study 1 (see section 4.1, above), in two visualization modes, 2D and 3D.

Participants. Seven male subjects with ABI, mean age of 28.6 years old (SD=8.1), mean education of 10 years (SD=1.5), were recruited.

Procedure. We tested the time spent in the tasks in each scenario (Scenario 1: storage room - recognition; Scenario 2: dining room - sorting; Scenario 3: bedroom - problem solving). Two evaluations were conducted four days apart (Test 1 vs Test 2). The virtual environments were visualized in a 3D projection screen (eyeglasses).

Table 2 - Time participants (P1 to P8) spent in the tasks by scenario and by visualization mode

	Scenario 1		Scenario 2		Scenario 3				
	2D (min)	3D (min)	2D (min)	3D (min)	2D (min)	3D (min)	M Test 1	M Test 2	Comparison M2D *vs* M3D
P1	2.85	3.70	4.65	5.18	6.08	2.12	4.53	3.67	Improved 19%
P2	1.12	3.60	0.92	0.80	2.22	0.73	1.42	1.71	Worsen 21%
P3	2.48	0.93	4.17	6.50	1.50	2.45	2.72	3.29	Worsen 21%
P4	1.65	2.02	1.42	1.02	5.67	1.37	2.91	1.47	Improved 50%
P5	6.00	5.42	17.50	2.08	7.00	2.05	10.17	3.18	Improved 69%
P6	2.48	3.20	1.17	1.07	2.43	1.63	2.03	1.97	Improved 3%
P7	2.07	2.95	2.35	2.33	1.50	1.55	1.97	2.28	Worsen 15%

Results and Discussion. Comparing with the 2D visualization mode, no significant improvement was observed in the 3D visualization mode in what concerns the necessary time to complete the tasks. However, the number of errors was lower for the 3D than for the 2D visualization mode. Regarding the VR technology potential concerning motivation towards the rehabilitation tasks, we observed good involvement of the subjects when browsing the VEs and performing the tasks in both visualization modes (2D and 3D). Also, they all gave equivalent positive answers to the questionnaire on satisfaction with the use of both visualization modes. The main difficulties in both modes seemed related to the simultaneous use of the mouse and the keyboard to navigate, because these are poorly fit to the physical disabilities that most subjects had. The main advantage that can be pointed out to the visualization in 3D was the dimension of objects and environments coming from the projection system; Interestingly, although subjects did not report a strong sense of immersion in the 3D visualization mode, the interest they expressed in taking part in future studies was higher for 3D than for 2D.

4.3 Study 3

Goal. To test the Training Program (assessment and rehabilitation phases), through the application of a usability test (System Usability Scale - SUS, Digital Equipment Corporation, 1986).

Participants. Nine subjects with ABI, 5 males (55.6%) and 4 females (44.4%), mean age of 28.1 years old (SD=5.4), mean education of 9 years (SD=4.1), were recruited.

Procedure. In this pilot test of the initial prototype, participants experimented one of the program's levels – to shop in the supermarket using a shopping list. They needed to navigate in the supermarket and acquire the specified products by clicking on them. Additionally, they were asked to identify the specified products.

Results and Discussion. The analysis revealed that all participants obtained scores above 40 (possible range varying between 0 and 80 in the SUS, due to the exclusion of items 5 and 6). These results above the scale's midpoint lend support to the usability of the program. The sample mean is 58.1% (SD=14.1%), which is a satisfactory result. Nevertheless the findings should be interpreted with caution, particularly with regard to the influence of item 4 on the global score ("I think that I would need the support of a technical person to be able to use this system"). The answer to this item may not always correspond to32 patients' real capacities, but to their personal perceptions of deficits. Given the pathologies in question, some lack of correspondence with reality is expected in this population. There may be either an ability overestimation or underestimation. The first one may occur as a result of self-awareness deficit; the second one may be due to generalization of the difficulties from some areas to others, almost as a form of learned helplessness. Closely related to this item's content is item 10 ("I needed to learn a lot of things before I could get going with this system"), in which assessment of the program seems to be very dependent on perceived self-efficacy. These two items correspond to the "Learnability factor" and the other eight to the "Usability factor" [35]. Thus, the "Learnability factor" is likely more susceptible to the influence of subjects' pathologies (although further analyses of these two factors as separate scales are needed). Non response to item 7 (i.e., rate of 3 in this item) ("I would imagine that most people would learn to use this system very quickly") was explained by subjects feeling that they cannot answer it, given the diversity of deficits each patient has. One extra item was added to the scale with the aim of assessing the role (relevance) of the VR program on motivation to participate in the rehabilitation process. In this item, respondents indicate the degree of relevance of the VR program to this end on a 5-point Likert scale (1 - nothing important; 5 - very important). All participants obtained scores above 3 (midpoint of the scale). This suggests that subjects recognize the relevance of the VR program on motivation to participate in the rehabilitation process.

5 Conclusion

In this paper we briefly contextualized the importance of SG in several domains, namely the area of health, and cognitive rehabilitation in particular. We introduced one of the issues that have recently been discussed in the literature and in our team: The balance between technologically advanced, "beautiful" tools still requiring considerable financial support to be implemented *versus* less expensive solutions which may nevertheless contribute to improvements in intervention and the scientific study of recovery mechanisms. Both require systematic research to become part of the rehabilitation process in a sustained manner.

Reflecting this concern, we presented the CARP-VR as an SG tailored to cognitive rehabilitation that did not involve expensive technological solutions and includes exercises that are theoretically grounded in the fields of Cognitive Psychology and Neuropsychology. The clinical experience of those involved in its design was also important for its conception and making. The program has been tested throughout its development process. Results in our pilot-studies with ABI patients are promising, supporting the usability of the VR program and showing its relevance in subjects' motivation to participate in the rehabilitation process, which also reflects their satisfaction with it.

Usability tests with other program levels and with a more advanced version of the program (that includes improvements resulting from the previous tests) are currently in progress. With the progression of the project we hope to contribute to the implementation of the SG to the cognitive rehabilitation field, promoting independence and functionality of ABI patients, thus improving their quality of life.

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III. Desenho e Validação de Paradigmas Experimentais

Artigo 8 - Amygdalae Activation to 2D and 3D Emotional Inducing Stimuli

Dores, A. R., Barbosa, F., Monteiro, L., Reis, M., Coelho, C. M., Ribeiro, E., Leitão, M., de Sousa, L., & Castro Caldas, A. (submetido). Amygdalae Activation to 2D and 3D Emotional Inducing Stimuli.

Amygdalae Activation to 2D and 3D Emotional Inducing Stimuli

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Abstract

This study compared differences between 3D and standard (2D) visual stimuli, organized in virtual reality scenarios of different valence (pleasant, unpleasant, neutral), in their effect on the activity of emotion-related brain areas through fMRI. Here we show that unpleasant and neutral stimuli activated the right amygdala stronger when presented in 3D, compared with 2D. These results suggest that 3D stimuli, when used as “building blocks” for virtual environments, can induce increased emotional loading, as it is here showed through neuroimaging.

Keywords: virtual reality; 3D/2D visual stimuli; valence (pleasant, unpleasant, neutral); amygdala, functional Magnetic Resonance Imaging (fMRI).

1. Introduction[14]

During the last decades many studies have been published concerning the neural basis of different emotional response systems (LeDoux, 1996; Panksepp, 1998) and their influence on cognitive processes such as attention (Lang, Bradley, & Cuthbert, 1997), memory (Ochsner & Schacter, 2000), or cognitive skills involving composite functions, such as decision making (Damásio, 1994). Most of these studies have applied emotion-inducing pictures in the context of laboratory experimentation. Functional Magnetic Resonance Imaging (fMRI) studies were particularly relevant for the study of emotions for this technique provided additional information about the neural substrates of the processing stimuli with emotional content. The increasing availability of fMRI has greatly stimulated this field of research. However, this form of exploration of emotional phenomena was mainly done using simple slide-like pictures or other simple stimuli to allow for added experimental control. This approach, nonetheless, encumbers participant sense of presence, which could be important to the purpose of inducing emotions.

Presence is a subjective perception in which the participant, through technology, engages in the task, becomes more involved with the objects and perceives the stimuli as if technology was not present (Slater, Perez-Marcos, Ehrsson, & Sanchez-Vives, 2009). For the sense of presence are necessary involvement and immersion. The use of 3D stereoscopic visualization is recognized for its role on the promotion the first-person immersive experience (Lourenço, Azeff, Sveistrup, & Levin, 2008).

In recent years the relationship between virtual reality (VR) and variables such as motivation (Lourenço, Azeff, Sveistrup, & Levin, 2008), arousal, persuasion and affect (Grigorovici, 2001) has been investigated. With regard to this last variable, functional neuroimaging provided strong support for the critical role of the amygdala in emotional processing. The role of this structure in negative emotions has long been recognized in literature (Fanselow & Gale, 2003; LeDoux, 2003). Nevertheless, their involvement in positive emotions only recently has been accepted (Murray & Ramage, 2000).

A recent large meta-analysis (Sergerie, Caroline, & Armony, 2008) demonstrated that processing stimuli with emotional content consistently activates the amygdalae. However, once again, the 148 studies selected for the analysis did not use 3D stimuli. Despite the fact that realistic environments are avoided, in detriment of experimental control, some researchers such as Hoffman and colleagues (2003) demonstrated the possibility of combining VR technology with fMRI. Hoffman's participants reported a strong sense of immersion during data acquisition, despite constraints such as immobilization and noise. Shortly after, Lee and colleagues (2005) studied the effect of 2D and 3D stimuli

[14] As referências bibliográficas deste artigo encontram-se no formato proposto pela revista a que foi submetido.

as cues for inducing smoking craving, and concluded that the latter produce greater activation in brain areas involved in attention, visual balance and movement coordination. To the best of our knowledge, except for the above-mentioned studies, there are no other studies comparing the effects of 2D with 3D emotion-inducing stimuli through measures of brain activation.

The investigation of emotions, their neural substrates and their effects on other mental functions, lacks optional stimuli, more able to optimize the induction of emotional responses in controlled laboratory settings, where it is possible to manipulate and quantify the experimental results. The use of VR technology contributes to this aim, enabling the development of stimuli with properties closer to the real ones. The three-dimensionality seems critical to confer an increased sense of presence to the emotional objects, enabling a better emulation of the reality in the laboratory environment (Coelho, Santos, Silvério, & Silva, 2006; Insko, 2003). Since 3D enhances the feeling of presence (Coelho, Tichon, Hine, Wallis, & Riva, 2006), we hypothesized that 3D stimuli will enhance the emotions conveyed by the projected images.

In this study, we have chosen the most pleasant, unpleasant and neutral stimuli from our database of 3D objects and evaluated brain activation when observing virtual scenarios comprising them in a functional MRI study. The main aim of the present research was to test the hypothesis that 3D stimuli produce greater activation in the amygdalae compared to the conventional 2D display, at least in the unpleasant condition, considering their role in the processing of aversive stimuli and in the recognition of unpleasant emotions, such as fear (Baxter & Murray, 2002).

The effects of three-dimensional stimuli on specific visual processing areas were not within our scope, even if a whole-brain analysis was also conducted. In this study we were particularly interested in comparing the BOLD signal changes in the amygdalae when participants were presented emotion-inducing stimuli in VR scenarios of different *valences* (pleasant, unpleasant, neutral), displayed in two visualization modes (2D, 3D).

2. Materials and Methods

2.1. Participants

Twelve healthy male subjects, all right handed (self-reported), were recruited and gave written informed consent before taking part in this study. The mean age was 26.58 years (*SD* = 5.16, range 18-35 years). None of the participants had any contraindication for MRI. Through a screening interview, pathologies of the Central Nervous System (CNS), psychiatric disorders, trauma, and visual acuity deficits were ruled out.

2.2. Materials

Each scenario (Figure 1) included sets of 15 stimuli-objects, one set per valence (3DAIS – 3D Affective Scenarios). Each of these stimuli were chosen from our database of 3D objects, developed after the ones of the International Affective Picture System – IAPS (Lang, Bradley, & Cuthbert, 1999) and previously validated with Self Assessment Manikin – SAM (Lang, 1980). The database was validated for emotional arousal and valence using similar rating procedures to Lang and colleagues (1999) in the development of the IAPS. The database comprises 131 3D objects, each rated by 214 individuals on the 9-point SAM scale for emotional arousal (1 - lower, 9 - higher) and valence (1 - unpleasant, 9 – pleasant) as reported by Monteiro, Barbosa and Silvério (2011).

The stimuli were chosen according to the following criteria: 1. the stimuli (n=15) that were scored highest in valence and arousal (valence ≥ 6.0; arousal ≥ 4.0) were grouped in pleasant condition; 2. the stimuli (n=15) scored lowest in valence but highest in arousal (valence ≤ 4.0; intensity ≥ 4.0) were grouped in unpleasant condition; 3. finally, the stimuli scored with intermediate values in the valence scale and low in arousal (valence ≥ 4.5 and ≤ 5.5, arousal ≤ 3.0) were grouped in the neutral emotional condition. The selected objects are described in Table 1.

Table 1 - *Selected objects for each scenario with the respective* arousal *and* valence scores.

Objects	Pleasant *M (SD)*		Objects	Neutral *M (SD)*		Objects	Unpleasant *M (SD)*	
	Arousal	Valence		Arousal	Valence		Arousal	Valence
Cocktail	7.99 (1.36)	5.84 (2.37)	Roll the dough	5.07 (1.56)	2.57 (2.09)	Droppings	1.44 (1.78)	6.89 (2.98)
Woman	6.27 (2.03)	5.50 (2.95)	Cookware	5.36 (1.95)	2.76 (2.23)	Old mobile	2.27 (1.85)	4.23 (2.12)
Champagne	7.46 (2.06)	5.26 (2.66)	Valance	5.02 (1.37)	1.99 (1.98)	Knife	2.76 (1.97)	4.90 (2.40)
Bag of money	6.98 (2.04)	5.52 (2.22)	Dryer	5.19 (1.59)	2.20 (1.78)	Syringe	2.18 (2.04)	4.82 (2.63)
Flower 3	7.14 (1.71)	5.16 (2.67)	Iron ironing	4.83 (1.66)	2.10 (2.08)	Dirty toilet	1.80 (1.23)	5.97 (2.61)
Cake	6.94 (2.26)	5.27 (2.71)	Cutlery	5.15 (1.70)	2.39 (2.01)	Mouse	2.22 (2.15)	5.11 (2.42)
Cake 2	6.67 (1.78)	4.49 (2.82)	Glass 2	5.11 (1.63)	1.88 (1.38)	Corpse	2.12 (1.92)	4.35 (2.62)
Butterfly 2	6.39 (2.01)	3.89 (2.31)	Glass	5.16 (1.72)	2.04 (1.46)	Dirty sink	2.46 (1.92)	4.66 (2.16)
Champagne	6.94 (1.77)	4.19 (2.55)	Books	5.24 (2.12)	2.21 (2.40)	Pistol	2.50 (2.21)	5.36 (2.68)
Chocolates	7.63 (1.76)	5.29 (2.61)	Shoes	5.12 (1.26)	1.77 (2.18)	Old couch	2.77 (2.46)	4.97 (2.63)
Lobster	7.33 (1.83)	5.89 (2.44)	Springs clothing	4.97 (1.61)	1.98 (1.39)	Old bed	2.43 (1.73)	5.21 (2.23)
Strawberries	7.45 (1.62)	5.26 (2.61)	Craps	4.89 (1.69)	2.28 (2.07)	Cobweb	2.49 (1.80)	5.03 (2.12)
Ice cream	7.11 (1.74)	5.10 (2.80)	Clock	5.12 (1.52)	2.21 (1.99)	Snake	1.45 (1.91)	6.85 (1.83)
Biscuits	7.01 (1.81)	4.65 (2.61)	Table	5.04 (1.48)	2.15 (1.83)	Fly	2.29 (1.94)	5.19 (2.58)
Beach	8.19 (1.31)	6.61 (1.63)	Fan	5.12 (1.53)	2.09 (1.72)	Spider	1.97 (2.40)	6.25 (2.45)

A stimulation unit (laptop computer running Windows Vista) connected to a rear projection system (multimedia projector XGA 1024x768 pixels and 2200 ANSI lumens) was used to present the scenarios (Figure 1) in a 150x100 cm screen.

The MR scanning was carried out using a 1.5 T scanner (MAGNETON, Sonata, Siemens) with a gradient of Max. Amplitude 40 mT/m, Min. Rise Time 200 µs, Max slew rate 200 T/m/s. Participants observed the screen through a mirror while lying in the scanner, with 3D visualization being achieved through anaglyph image technique and the use of passive glasses (Zone, 2005).

Figure 1. Emotion-inducing scenarios of different valences (pleasant, neutral, unpleasant), which were projected in 2D and 3D.

2.3. Procedure

We implemented a simple 3x2 experimental design, within subjects, with *emotional valence* (pleasant, neutral, unpleasant scenario) and *visualization mode* (2D, 3D) as factors.

A block-design paradigm with two fMRI runs was used: one for the 2D scenarios and the other for the 3D scenarios (counterbalanced). There was no interval between runs, except the time that was necessary for participants to put or take the anaglyph glasses off, depending on the initial visualization condition (2D or 3D).

Both runs consisted of three cycles of rest and activation, one for each emotional valence (counterbalanced), with no interval between cycles. During resting periods a fixation cross was displayed for 40 sec, immediately followed by one of the scenarios. Each run was preceded by four seconds of no stimulation, which were discarded to allow for the MR signal to reach its equilibrium. Thus, the duration of a whole run was 4’4’’, as represented in Figure 2.

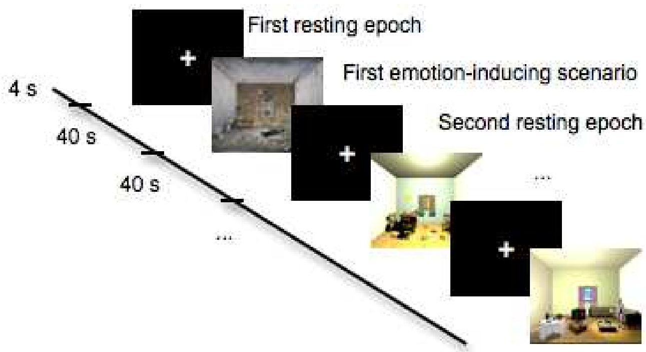

Figure 2. Schematic representation of one of the runs of the experimental paradigm.

During data acquisition, participants' heads were positioned in a standard radiofrequency head coil (equipped with a mirror) with tape and cushioning to minimize head motion. Participants were instructed to keep their eyes open during all session and pay attention to the image that was projected on the screen.

2.4. Data acquisition

For functional imaging a gradient–echo T2*-weighted Echo-Planar Imaging (EPI) sequence (TE=50ms, flip angle 90º, TR=4s) was used to measure the BOLD (blood oxygenation level dependent) effect (Ogawa et al., 1990). The Field of View (FOV) was 240 x 240mm2 with a 64 x 64 matrix resulting in an effective resolution of 3.75mm x 3.75mm x 3mm(Thk). Sixty volumes with 36 slices each were acquired in axial orientation with slices being aligned parallel to the anterior–posterior commissure. The slice thickness was 3mm with a gap of 25%. For anatomic reference, a high-resolution MPRAGE T1-weighted scan was acquired for each participant with the following parameters: TR = 2s, TE = 3.69ms, 256 x 256 matrix, FOV 240 x 240mm^2, slice thickness 1mm leading to an effective resolution of 0.9 x 0.9 x 1 mm).

2.5. Data analysis

Data preprocessing was performed using SPM8 (Wellcome Trust Centre for Neuroimaging, UCL, London, UK) running on MATLAB 2008A (The MathWorks Inc., Natick, MA, USA). The functional scans were realigned to correct for bulk motion of the head. After coregistration of functional and anatomical scans the data were normalized to the MNI standard brain (Montreal Neurological Institute, Montreal, Canada) using SPM's segment function. Finally, the functional data were smoothed with an 8x8 mm isotropic Gaussian kernel. A GLM-based fixed effects analysis was run on the data using SPM8. Movement parameters were used as regressors of no interest in the analysis. A region of interest (ROI) analysis was carried out for both amygdalae. The ROI was created using the Harvard-Oxford cortical and subcortical structural atlas (Harvard Center for Morphometric Analysis, Boston, MA, USA). Results were corrected for multiple comparisons using FWE (family-wise error) correction. A p-value of 0.05 was considered significant. In addition, whole brain results were calculated for all contrasts. An uncorrected p-value of 0.001 was considered significant in this case.

3. Results

ROI analysis showed a significant activation of the right amygdala for the neutral scenario in the contrast 3D > 2D (p = .016, FWE-corrected, 20mm -2mm -26mm) (Figure 3).

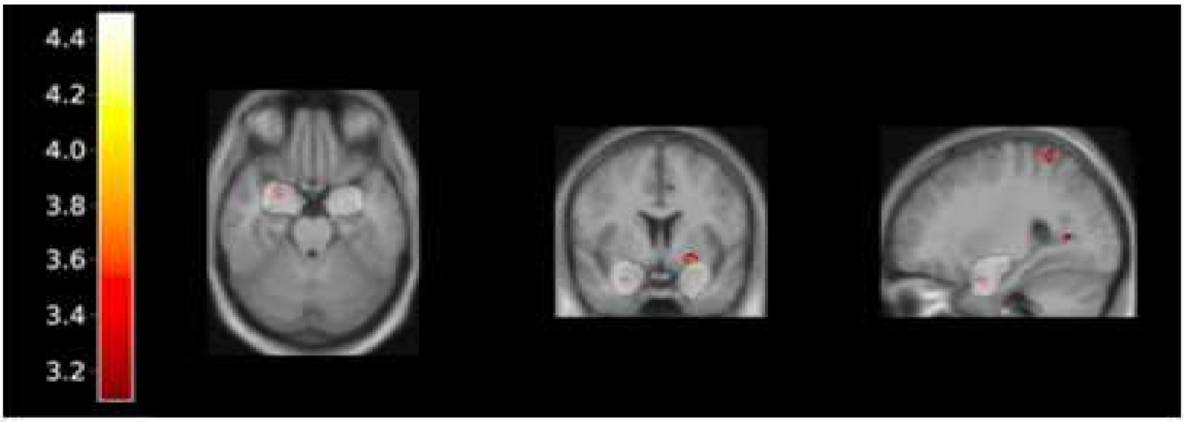

*Figure 3***.** ROI neutral 3D > 2D.

For the unpleasant scenario (Figure 4) there was a similar tendency with the right amygdala showing a marginally significant increased activation for the 3D visualization mode in comparison to the 2D scenario (p = .062, FWE-corrected, 26mm -10 mm -10 mm).

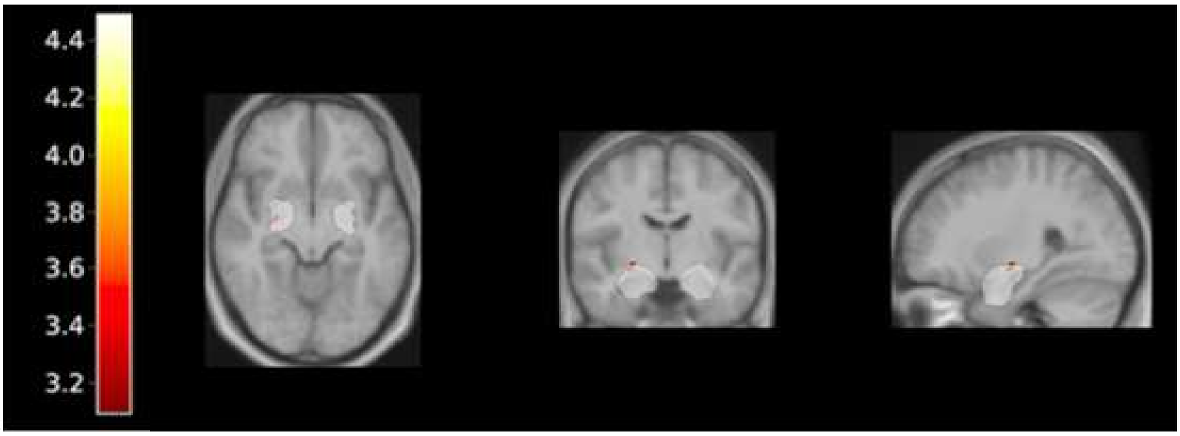

Figure 4. ROI unpleasant 3D > 2D.

At the whole brain level we found significant activations (*p* = .012, FWE- corrected and *p* = .049, FWE-corrected) for the contrast 3D>2D within the neutral condition respectably in the left rolandic operculum (-40mm -6mm 12mm) and in the right postcentral gyrus (62mm 0mm 14mm). No significant activations were found for the opposite contrast (2D>3D) or for other emotional conditions.

4. Discussion

Adding a third dimension to certain virtual scenarios seems to produce augmented activation in some brain regions. This study found increased activation of the right amygdalae, particularly in the neutral and unpleasant 3D scenarios. This suggests that the higher realism and presence of the 3D specific stimuli upregulates the amygdala response.

The right amygdala activation in the unpleasant 3D scenario corroborates previous studies that show right hemisphere dominance in the processing of negative emotions (Davidson, Ekman, Saron, Senulis, & Friesen, 1990). However, the increased amygdala activation for the neutral condition was not expected. This finding can result from specific meaning and/or somatosensorial-inducing features of the contents of the neutral scenario, considering that the same pattern of higher brain activation for the neutral 3D scenario when compared with the homologous 2D was also found in the left rolandic operculum (LRO) and in the right postcentral gyrus. This explanation would concur with the functional roles of these last brain structures, namely the involvement of the LRO in the encoding of language elements and their somatosensorial importance, but this explanatory hypothesis ought to be confirmed with further studies and increased samples.

Since this is a initial study in a series, in future studies we will consider other areas such as early visual association cortices that process different aspects of 2D *vs* 3D stimuli, and limbic cortex for emotion. Nevertheless, considering the existing literature, these results already contribute to enlighten the potential benefits of using virtual scenarios, comprising 3D objects, in the research of emotions.

Acknowledgments

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Artigo 9 – Effects of Emotional Valence and Three-dimensionality of Visual Stimuli on Brain Activation: an fMRI Study

Dores, A. R., Almeida, I., Barbosa, F., Castelo-Branco, M., Monteiro, L., Reis, M., de Sousa, L., & Castro Caldas, A. (submetido). Effects of Emotional Valence and Three-dimensionality of Visual Stimuli on Brain Activation: an fMRI Study.

Effects of Emotional Valence and Three-dimensionality of Visual Stimuli on Brain Activation: an fMRI Study

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Abstract

Examining changes in brain activation associated with emotion-inducing stimuli is essential to the study of emotions. Due to the ecological potential of virtual reality, inspection of whether brain activation in response to emotional stimuli can also be modulated by the three-dimensional properties of the images is now important. This study sought to test whether the activation of brain areas involved in the emotional processing of scenarios of different valences can be modulated by three-dimensionality. It focused on the interaction effect among emotion-inducing stimuli of different *emotional valences* (pleasant, unpleasant and neutral valences) and *visualization types* (2D, 3D). The effects of these variables and their interaction were analyzed through a 3x2 repeated measures *ANOVA*. Post-hoc *t*-tests were performed under a ROI-analysis approach. The results show increased brain activation for the 3D affective-inducing stimuli in comparison with the same stimuli in 2D scenarios, mostly in cortical and subcortical regions that are related to emotional processing, in addition to visual processing regions. This study might enable us to clarify brain mechanisms involved in the processing of emotional stimuli (scenarios' valence) and their interaction with three-dimensionality.

Keywords: emotional valence (pleasant, unpleasant, neutral); 3D/2D visual stimuli; functional Magnetic Resonance Imaging (fMRI).

1. Introduction[15]

Knowledge about emotions resulted largely from studies using images with emotional content in the context of laboratory experimentation. In constant development, the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1999) is one of the most widely used instruments for the selection of images. It now includes more than 900 emotional pictures in digital format, indexed by emotional valence, arousal and dominance, from various semantic categories: animals, landscapes, weapons, human facial expressions, mutilated bodies, etc. The emotional arousal and valence induced by the images have been measured through the *Self-Assessment Maniquin* (SAM; Lang, 1980).

However, the visualization of two-dimensional (2D) images as a method to induce emotions has some methodological limitations. Indeed, the laboratory investigation of emotional phenomena using simple slideshows containing drawings, words or images from the IAPS or similar systems has limited ecological validity and produces an attenuated emotional resonance in comparison to real emotional situations (Monteiro, Barbosa, & Silvério, in press). Thus, any development of these stimulus-materials making them closer to real emotional conditions is highly valuable to research. Still, stimuli must enable experimental manipulation of emotional responses in controlled laboratory sets. Adding three-dimensional (3D) properties to emotion-inducing stimuli is one method to achieve this purpose, making emotional responses more realistic.

Nowadays there are 3D softwares like Blender (Blender Foundation/Institute Amesterdan), 3ds Max (Autodesk, California) or Maya (Autodesk, California), that can generate stereoscopic images of great realism. The stimuli developed with those technologies are much more than simple slide-like pictures. They are equally easy to handle and present greater ecological validity than traditional stimulus-material, precisely because they are closer to real-life stimuli (Dyck, Winbeck, Leiberg, Chen, & Mathiak, 2010). For instance, Dyck and colleagues (2008) compared the recognition of 3D facial expressions (virtual expressions - avatars) with conventional photographs of human faces and found that sadness and fear were more easily recognized when presented in 3D. The work of Lee, Lim, Wiederhold, and Graham (2005) is another example. The authors investigated the effect of the two types of visualization on craving-inducing cues and concluded that participants show more attention to 3D than 2D stimuli. New 3D stimuli may thus represent a considerable benefit to emotion research in controlled laboratory environments. However, these new materials and their advantages over the conventional

[15] As referências bibliográficas deste artigo encontram-se no formato proposto pela revista a que foi submetido.

ones must be further investigated, either through self-report studies on the induced emotional states, and through studies on the respective neuronal correlates.

Functional neuroimaging supports the involvement of the amygdalae, fusiform gyri, inferior occipital gyri, orbital gyri, parahippocampal gyri, posterior cingulate cortex, and uncus as part of the neural systems in emotional processing (Adolphs, 2002, 2003; Adolphs, Damasio, Tranel, & Damasio, 1996; Jehna et al., 2011; Lane et al., 1997; Whalen, Rauch, Etcoff, McInerney, Lee & Jenike, 1998). The role of the amygdalae in negative (Fanselow & Gale, 2003; LeDoux, 2003) and positive emotions has been recognized in literature (Murray & Ramage, 2000). The role of the anterior insula (Craig, 2002, 2003; Critchley, Wiens, Rotshtein, Ohman, & Dolan, 2004) and of the anterior cingulated cortex (Decety & Jackson, 2004; Jackson, Brunet, Meltzoff, & Decety, 2006) in the processing of contexts perceived as emotionally salient is also well established. The contribution of basal ganglia and cerebellar regions to human affective function is also recognized (Baumann & Mattingley, 2012; Lane et al., 1997; Paradiso, et al., 1999).

In order to inspect the role of higher cortical mechanisms involved in emotional processing, we apply a paradigm in which subjects were involved in a long and repeated stimuli exhibition in order to create visual habituation. This procedure is intended to reduce the contribution of the low level visual processing mechanisms to the targeted contrasts, while emphasizing the relevance of the higher cortical mechanisms involved in emotional processing. We expect to find increased activation for the 3D affective-inducing stimuli in comparison with the same stimuli in 2D scenarios, mostly in cortical and subcortical regions that are related to emotional processing, in addition to visual processing regions.

2. Materials and Methods

2.1. Participants

The sample consisted of 12 healthy male subjects who were recruited to participate in the study from rehabilitation institutions' databases where they were registered as caregivers of former patients. The group's mean age was 26.58 years old (*SD* = 5.16). Participants were all right handed (self-reported) and had no contraindication for MRI, or pathologies of the Central Nervous System (CNS), psychiatric disorders, trauma, and visual acuity deficits (assessed through a screening interview). All gave written informed consent to participate in this study. The protocol was approved by the Local Ethics Committee, and complies with the Declaration of Helsinki.

2.2. Stimuli

The stimuli were three 3D Affective Inducing Scenarios (3DAIS) composed by 3D objects that were selected from our database, which comprises 131 objects. Sets of 15 stimuli-objects formed each scenario (Figure 1), with one set per *emotional valence* – pleasant, unpleasant and neutral (to view the final scenarios and the stimuli-objects, see Monteiro, Barbosa, & Silvério, in press). The 3D objects database had been previously developed according to the type of contents in the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1999) and validated with the *Self-Assessment Maniquin* (SAM; Lang, 1980) through rating procedures similar to those Lang and colleagues (1999) employed in the IAPS. For our database, 214 individuals rated each of the 3D objects on the 9-point SAM scale for emotional arousal (1 - low, 9 - high) and valence (1 - unpleasant, 9 – pleasant) (Monteiro, Barbosa, & Silvério, in press).

The stimuli were then selected and grouped according to the following criteria: (a) fifteen 3D objects receiving the highest scores in valence and arousal (valence ≥ 6.0; arousal ≥ 4.0) were included in the pleasant scenario; (b) fifteen 3D objects receiving the lowest scores in valence and the highest in arousal (valence ≤ 4.0; arousal ≥ 4.0) were included in the unpleasant scenario; (c) fifteen stimuli with intermediate values in valence and low scores in arousal (4.5 ≤ valence ≤ 5.5, arousal ≤ 3.0) were included in the neutral scenario.

Scenarios, occupying a visual angle of 32º x 22º, were presented in a 150x100 cm screen with a stimulation unit (laptop computer running Windows Vista) connected to a rear projection system (multimedia projector XGA 1024x768 pixels and 2200 ANSI lumens).

A 1.5 T scanner (MAGNETON, Sonata, Siemens) with a gradient of Max. Amplitude 40 mT/m, Min. Rise Time 200 µs, Max slew rate 200 T/m/s, was used for the MR scanning. Participants lay in the scanner, viewing the screen through a mirror, and used passive glasses (Zone, 2005) for 3D visualization, created through an anaglyph image technique.

*Figure 1***.** Emotion-inducing scenarios of different valences (pleasant, neutral, unpleasant), which were projected in 2D and 3D.

2.3. Design and Procedures

Visualization type (2D, 3D types) and *emotional valence* (pleasant, unpleasant and neutral scenarios) were used as factors in a simple within-subjects 3x2 experimental design. The experiment consisted of a single session of fMRI scanning. The presentation of the 2D and of the 3D scenarios was counterbalanced in a block-design paradigm with two fMRI runs for the two *visualization types*, respectively. The duration of a whole run was 4’4’’. Four seconds of no stimulation (then discarded) preceded each run to allow for the MR signal to reach the equilibrium point. Participants had the necessary time to put on or take off the anaglyph glasses between runs, to match the initial visualization condition (2D or 3D types). Each run consisted of three cycles of rest and activation with no interval between cycles. The three cycles corresponded to the three *emotional valences*, also counterbalanced to control order effects. During resting periods a fixation cross was displayed for 40 sec, followed immediately by one of the scenarios, also displayed for 40 sec.

For data acquisition, participants’ heads were positioned in a standard radiofrequency head coil (equipped with a mirror) with tape and cushioning to minimize head motion. Participants were instructed to avoid moving, to keep their eyes open during all session, and pay attention to the image projected on the screen.

2.4. Data acquisition

For functional imaging a gradient–echo T2*-weighted Echo-Planar Imaging (EPI) sequence (TE=50ms, flip angle 90º, TR=4s) was used to measure the BOLD (blood oxygenation level dependent) effect (Ogawa, Lee, Kay, & Tank, 1990). The Field of View (FOV) was 240 x 240mm2 with a 64 x 64 matrix resulting in an effective resolution of 3.75mm x 3.75mm x 3mm(Thk). Sixty volumes with 36 slices each were acquired in axial orientation, with slices being aligned parallel to the anterior–posterior commissure. The slice thickness was 3mm with a gap of 25%. For anatomic reference, a high-resolution MPRAGE T1-weighted scan was acquired for each participant with the following parameters: TR = 2s, TE = 3.69ms, 256 x 256 matrix, FOV 240 x 240mm^2, slice thickness of 1mm leading to an effective resolution of 0.9 x 0.9 x 1 mm).

2.5. Data analysis

Preprocessing of functional data, including slice time correction, 3D motion correction, spatial smoothing and temporal filtering, was conducted using BrainVoyager QX 2.3 (2011, Brain Innovation, Netherlands). Functional and anatomical scans of the data were co-registered and normalized to Talairach space. Data were analyzed through a GLM-based random effects procedure. Resulting whole brain activation maps for all contrasts were thresholded at p-value < 0.001 (uncorrected). We accepted only clusters consisting of at least seven contiguous voxels.

The effects of *emotional valence* (pleasant, unpleasant and neutral scenarios), the *visualization type* (2D and 3D types), and their interaction were computed through a 3x2 repeated measures *ANOVA*. Post-hoc *t*-tests were performed under a ROI-analysis approach on the clusters for which the ANOVA showed significant interaction effects. Talairach Client, version 2.4.2 was used to convert coordinates of the regions significantly activated into Talairach labels that were within the voxel size (Lancaster et al., 1997; Lancaster et al., 2000).

3. Results

The ANOVA showed an interaction effect between *emotional valence* (pleasant, unpleasant and neutral scenarios) and *visualization type* (2D and 3D types). Table 1 lists the areas that were activated for this effect. Table 2 shows the post-hoc tests comparing *emotional valences* within *visualization types* (unpleasant vs. pleasant vs. neutral scenarios within the 2D type, and unpleasant vs. pleasant vs. neutral scenarios within the 3D type) and *visualization types* within *emotional valences* (3D vs. 2D types within the pleasant scenario, 3D vs. 2D types within the unpleasant scenarios, and 3D vs. 2D types within the neutral scenarios).

Table 1
Anatomic location, brain hemisphere, brain areas and their Talairach coordinates, in which seven or more voxels were activated, detected through 3x2 ANOVA analysis: *Interaction effect of* visualization effects *and* valence*.*

Anatomic Location	**BH**	**BA**	**Coordinates**			***F***	***P***	**Size**
			x	**y**	**Z**			
Uncus	L	36	-19.0	-8.0	-27.0	18.506	0.000019	31
Postcentral Gyrus	R	3	41.0	-20.0	51.0	13.294	0.000164	20
Middle Frontal Gyrus	R	46	53.0	28.0	24.0	16.225	0.000047	15
Declive	R		35.0	-62.0	-15.0	16.723	0.000038	15
Cerebellar Tonsil	L		-37.0	-38.0	-36.0	15.234	0.000070	14
	L		-25.0	-41.0	-42.0	15.584	0.000061	13
	L		-13.0	-56.0	-36.0	14.638	0.000091	8
Cingulate Gyrus	R	24	20.0	-8.0	39.0	15.697	0.000058	10
Lentiform Nucleus	L		-31.0	-14.0	6.0	15.336	0.000067	9

Note: BH = Brain Hemisphere; BA = Brodmann's area; L = left; R = right; *number of voxels.

Table 2
Random effects analysis of contrasts: Post-hoc t-*tests to identify (a)* valence effects (Pl, Unpl and N valences) *within* visualization type (2D, 3D types) and (b) visualization effects *within* valence.

Contrast	**df**	***t***	***P***	**Coordinates**			**Anatomic Location**
Valence effects within *visualization type* (a)				**X**	**Y**	**z**	
2D Unpl > 2D Pl	11	4.554	.001	-19.0	-8.0	-27.0	Uncus
2D Pl > 2D N	11	3.499	.005	41.0	-20.0	51.0	Postcentral Gyrus
2D Unpl > 2D N	11	5.859	.000				
3D Pl > 3D N	11	3.483	.005	53.0	28.0	24.0	Middle Frontal Gyrus
2D Unpl > 2D N	11	3.830	.003	-37.0	-38.0	-36.0	Cerebellar Tonsil
2D Pl > 2D N	11	3.391	.006	-25.0	-41.0	-42.0	
2D Pl > 2D N	11	3.400	.006	20.0	-8.0	39.0	Cingulate Gyrus
2D Unpl > 2D N	11	4.015	.002				
Visualization effects within *valence* (b)							
3D > 2D Pl	11	2.985	0.012	35.0	-62.0	-15.0	Declive
3D < 2D N	11	3.611	0.004	-13.0	-56.0	-36.0	Cerebellar Tonsil

Note: Pl = pleasant; Unpl = unpleasant and N = neutral. The results are corrected for multiple comparisons, (a) p = .05/6 <.008, (b) p = .05/3 <.017.

Concerning the main effects, volumes-of-interest were created for each cluster (minimum size = 7 voxels) after the 3x2 *ANOVA*, and *post-hoc t-tests* were performed under a ROI-analysis approach. Results for *emotional valence* are presented in Table 3.

Table 3.
Anatomic location, brain hemisphere, brain areas and their Talairach coordinates in which seven or more voxels were activated, detected through 3x2 ANOVA analysis and post-hoc t-*tests: Main effect of* emotional valence.

Anatomic Location	**BH**	**BA**	**Coordinates**						**Contrast**			
			X	**y**	**Z**	***F***	***P***	**Size***		***t***	**df**	***P***
Paracentral Lobule	L	5	-10.0	-41.0	60.0	18.957	0.000016	20	Unpl > N	5.084	11	.000
									Unpl > Pl	3.611	11	.004
Inferior Parietal Lobule	R	40	41.0	-47.0	55.0	12.306	0.000259	15	Pl > N	3.572	11	.004
									Unpl > N	4.496	11	.001
	R	40	47.0	-29.0	48.0	14.521	0.000095	7	Unpl > N	3.759	11	.003
									Unpl > Pl	4.637	11	.001
Precuneus	L	7	-31.0	-44.0	51.0	14.190	0.000110	11	Pl > N	3.515	11	.005
									Unpl > N	2.820	11	.017
									Unpl > Pl	4.458	11	.001
Superior Temporal Gyrus	R	22	62.0	-35.0	9.0	13.985	0.000120	9	Pl > N	2.985	11	.002
									Unpl > N	5.056	11	.000
									Unpl > Pl	3.274	11	.007

Middle Frontal Gyrus	R	10	32.0	34.0	18.0	14.519	0.000095	9	Unpl > N	4.441	11	.001
									Unpl > Pl	4.878	11	.000
Postcentral Gyrus	R	3	62.0	-11.0	24.0	14.828	0.000084	8	Unpl > N	5.740	11	.000
									Unpl > Pl	5.386	11	.000

Note: BH = Brain Hemisphere; BA = Brodmann's area; Pl = pleasant; L = left; R = right; N = neutral; Unpl = unpleasant; *number of voxels. The results are corrected for multiple comparisons.

Additionally, a main effect of *visualization type* was found on several areas, as reported in Table 4.

Table 4.
Anatomic location, brain hemisphere, brain areas and their Talairach coordinates in which seven or more voxels were activated, detected through 3x2 ANOVA analysis and post-hoc t-tests: Main effect of visualization type.

Anatomic Location	**BH**	**BA**	**Coordinates**						**Contrast**			
			X	**y**	**Z**	***F***	***P***	**Size***		***t***	**df**	***P***
Lentiform Nucleus	L		-16.0	-2.0	-6.0	43.408	0.000039	38	3D > 2D	6.750	11	.000
Fusiform Gyrus	L	20	-55.0	-35.0	-21.0	45.157	0.000033	25	3D > 2D	6.372	11	.000
	L	20	-43.0	-8.0	-24.0	33.798	0.000117	18	3D > 2D	5.168	11	.000
Precentral Gyrus	L	6	-49.0	-2.0	33.0	47.479	0.000026	22	3D > 2D	3.901	11	.002
	R	6	32.0	-14.0	54.0	32.910	0.000131	10	3D > 2D	6.085	11	.000
Cuneus	L	17	-19.0	-95.0	0.0	48.263	0.000024	20	3D > 2D	3.571	11	.004
Superior Temporal Gyrus	L	42	-52.0	-32.0	15.0	35.788	0.000092	16	3D > 2D	5.369	11	.000
Precuneus	L	31	-13.0	-62.0	21.0	32.412	0.000140	14	3D > 2D	5.440	11	.000
	L	7	-19.0	-71.0	48.0	32.241	0.000143	14	3D > 2D	5.003	11	.000
	L	7	-1.0	-53.0	39.0	27.216	0.000287	13	3D > 2D	6.104	11	.000
Middle Frontal Gyrus	L	9	-46.0	31.0	30.0	26.381	0.000325	12	3D > 2D	5.490	11	.000
Inferior Frontal Gyrus	R	45	50.0	22.0	12.0	29.854	0.000197	7	3D > 2D	5.346	11	.000
Superior Frontal Gyrus	R	6	5.0	7.0	57.0	30.968	0.000169	7	3D > 2D	4.141	11	.002
Superior Temporal Gyrus	R	38	47.0	7.0	-18.0	29.348	0.000211	7	3D > 2D	4.572	11	.001
Cuneus	L	17	-16.0	-80.0	6.0	29.755	0.000199	7	3D > 2D	5.417	11	.000
Sub-Gyral	L	40	-31.0	-44.0	33.0	29.261	0.000214	7	3D > 2D	4.759	11	.001

Note: BH = Brain Hemisphere; BA = Brodmann's area; L = left; R = right; *number of voxels. The results are corrected for multiple comparisons.

4. Discussion

Our purpose was to test whether the activation of brain areas involved in the emotional processing of scenarios of different valences can be modulated by three-dimensionality and to study the role of cortical mechanisms involved in emotional processing. We compared BOLD signal changes in emotional areas and visual areas, in addition to areas responsible for cognitive functions, when participants were presented with VR scenarios in two different *visualization types* (2D and 3D types).

The most interesting finding refers to the interaction effect between *emotional valence* and *visualization type* in areas responsible for emotional and cognitive processing. As expected, we found increased activation in cortical areas, such as the postcentral gyrus and middle frontal gyrus, but only with pleasant and unpleasant scenarios. The involvement of these regions has been previously identified in neuroimaging studies of emotion (Damasio et al., 2000, George, Ketter, Parekh, Herscovitch, & Post, 1996; Lane, Chua, & Dolan, 1999), and the activated prefrontal region may reflect the presence of high-level cognitive interpretations (Ochsner et al., 2009). We expected that these areas would be elicited by the paradigm used, which consisted of a long and repeated stimuli exhibition. The results also show the activation of subcortical structures, such as some components of the cerebellum (i.e., the declive and cerebellar tonsil) and some components of the basal ganglia (i.e., the lentiform nucleus, which refers to the globus pallidus and the putamen) (Baumann & Mattingley, 2012; Lane et al., 1997; Paradiso, et al., 1999). The cerebellum only recently have started to be recognized as part of the neural pathways responsible for emotional processing (Baumann & Mattingley, 2012; Tettamanti, et al., 2012), although its role in emotion is still unclear. In addition to these regions, we found the activation of portions of the limbic lobe (i.e., the uncus [Lawrenceet al., 2994] and cingulated gyrus [Decety & Jackson, 2004; Jackson, Brunet, Meltzoff, & Decety, 2006]), traditionally recognized as especially significant for emotion. Considering that current neurobiological models of emotion and several studies (Baumann & Mattingley, 2012; Kober, et al., 2008; Tettamanti, et al., 2012) recognize the mediation of cortical and subcortical areas in emotional processing these results are consistent with the literature.

Concerning the *valence effects* within *visualization type*, the results that allowed us to understand the relation between the different emotional valences indicate that the direction of the contrasts was as expected, i.e., unpleasant>pleasant>neutral valence for the 2D visualization type, but only pleasant>neutral for the 3D visualization type. The direction of the contrasts was clearer when we examined the *emotion valence* independently of the *visualization type* (the main effect of *emotion valence*). In this case, the well-known unpleasant emotion bias seems to be present in our fMRI data, as unpleasant scenarios produce higher activation than the pleasant and neutral ones in all the referred brain regions, namely the paracentral lobule, inferior parietal lobule, precuneus, superior temporal gyrus, middle frontal gyrus and postcentral gyrus. We also found differences between pleasant and neutral scenarios for the inferior parietal lobule, superior temporal gyrus and precuneus, with the former producing higher activation of these areas. In some of these areas (inferior parietal lobule, precuneus, superior temporal gyrus) we also observed that pleasant scenarios elicited more activation that neutral ones.

Concerning the visualization effects *within* valence, post-hoc analyses revealed that 3D only produces greater activation than 2D for the pleasant valence, in the declive. Unexpectedly, we found the opposite effect for the neutral scenario, in the cerebellar tonsil. When we examined the results of the main effect of *visualization* type (independently of emotional valence), the 3D consistently produced greater activation than the 2D, in all activated brain regions.

Further research is necessary to understand these results, mainly when the two variables, *emotional valence* and *visualization type*, are in interaction. The use of a larger sample may be important for this purpose.

Finally, the results also show the influence of three-dimensional scenarios on visual processing, although this was not the main focus of this study. Specifically, 3D scenarios produced an increased activation in regions that are part of the anterior intraparietal area (Precuneus [BA 7, 31] and Sub-Gyral [BA 40]) and inferotemporal cortex (Fusiform Gyrus [BA 20]). These results are consistent with the literature that reports the involvement of these regions in visual processing of 3D stimuli. An example of this phenomenon is the participation of AIP neurons in the perception of 3D contours and surfaces (Theys, Srivastava, van Loon, Goffin, & Janssen, 2012) or the involvement of the IT cortex in the perception of binocular disparity (Janssen, Vogels, & Orban, 2000; Uka, Tanabe, Watanabe, & Fujita, 2005; Verhoef, Vogels, & Janssen, 2012).

The observed activation of the Precuneus (BA 7) also supports the role of 3D in stereopsis, since this area has been connected with this function (Fortin, Ptito, Faubert, & Ptito, 2002). This region is more activated with 3D than with 2D stimuli in our study. Part of the primary visual cortex, the V1 (cuneus or BA 17) was activated.

Summing up, these preliminary fMRI results suggest that 3D scenarios may be useful in methodological paradigms for the experimental research of emotions. They may represent an advantage when compared to 2D stimuli, as they bring more realism into laboratorial settings.

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Artigo 10 - An fMRI Paradigm Based on Williams Inhibition Test to Study the Neural Substrates of Attention and Inhibitory Control

Dores, A. R., Barbosa, F., Carvalho, I. P., Almeida, I., Guerreiro, S. Martins da Rocha, B., Cunha, G., Castelo Branco, M., de Sousa, L., & Castro Caldas A. (submetido). An fMRI paradigm based on Williams Inhibition Test to study the neural substrates of attention and inhibitory control.

An fMRI paradigm based on Williams Inhibition Test to study the neural substrates of attention and inhibitory control

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Abstract

The purpose of this study is to present a paradigm, based on the Williams Inhibition Test (WIT), to study attentional and inhibitory control and their neuroanatomical substrates. Although previous imaging studies have analyzed brain activation with experimental paradigms based on Stroop and Simon tasks, which present some similarities to the WIT, this last one is more demanding, and there is still no evidence from neuroimaging of the activated areas during its performance, or of whether it allows discrimination of performances between healthy and clinical populations.

With these needs in mind, in the present study we analyze the BOLD signal in 10 healthy participants performing the WIT. The Dorsolateral Prefrontal Cortex (DLPFC) (Brodmann's areas [BAs] 9/46), the Inferior Prefrontal Cortex (IFC; BA 44), the Anterior Cingulated Cortex (ACC; BA 32), and the Posterior Cingulated Cortex (PCC; BA 6) were defined for specified region of interest (ROI) analysis. We additionally compare behavioral data (hits, errors, reaction times) of the healthy participants with those of eight Acquired Brain Injury patients. Data were analyzed with GLM-based random effects and Mann-Whitney tests.

Results show the involvement of the defined regions and indicate that the WIT is sensitive to brain lesions, suggesting that this WIT-based block design paradigm can be used as a research methodology for behavioral and neuroimaging studies of the attentional and inhibitory components of executive functions.

Keywords: *Williams Inhibition Test* (WIT); Functional MRI; Behavioral performance; Prefrontal cortex, Attentional control; Inhibitory control.

1. Introduction[16]

We can find dozens of definitions and more than 33 components of executive functions in the literature today (Barkley, 2011). Lezak coined the term "executive function", referring to those skills involved in the formulation of goals, in the planning of strategies to achieve those goals, and in self-evaluations during these activities (Lezak, 1982, 1987). The author viewed the concept in terms of four components: volition, planning, purposive action, and effective performance (Lezak et al., 2004). Evidence from neuropsychology, neuroimaging and pathophysiology increasingly supports the idea that this is not a unitary concept, and the assessment of executive functions remains a current challenge (Lezak, 1982; Marcotte and Grant, 2010; Oddy and Worthington, 2009). Different studies have systematized and critically analyzed the instruments used in the neuropsychological assessment of executive functions (e.g., Marcotte and Grant, 2010; Murray and Ramage, 2000; Pickens et al., 2010). One of the identified limitations is that the evaluation is almost always carried out in conditions where diverse executive functions' components are used, which raises the issue of what is really being assessed (Odhuba, 2005).

Attentional and inhibition control seem to be two key components of executive functions (e.g., Ylvisaker, 1998). They are involved in solving new, unusual or complex problems, namely when it is necessary to choose between different strategies of action which may be competing with that goal-oriented one that would be the best. Additionally, even when the best alternative is chosen, it can become inadequate in changing contexts, which force the replacement of automatic behaviors by more adequate responses. Thus, while attentional control ensures that current actions are consistent with the established goals, automatic response inhibition is a central process of self-control, and both are part of the executive functions. Independent, adaptive, and socially integrated functioning is a result of these processes.

Attentional and inhibitory control have been evaluated through Simon- or Stroop-like tasks (Liu et al., 2004). However, these tasks are too structured, repetitive, and always present the same degree of difficulty. These characteristics are ill-suited to fit the properties of executive functioning, which involve novelty, cognitive flexibility and adaptability to task changes. In addition to these limitations, the specificities of each task (e.g., its semantic content) may involve other cognitive processes, as in the case of the Stroop task, complicating the discrimination of brain areas responsible for attentional and inhibitory control (Nee, 2007). Another commonly used strategy to study these components is the Go/No-Go paradigm. However, the differences found in the brain areas

[16] As referências bibliográficas deste artigo encontram-se no formato proposto pela revista a que foi submetido.

activated with Go/No-Go stimuli can, like the tasks mentioned above, reflect processes other than attentional and inhibitory control (Forstmann et al., 2008; Garavan et al., 2002).

Some works have attempted to disentangle the effects of the cognitive task itself from the stimulus material used in the study of brain activation. For example, Hazeltine et al. (2003) recognize that the activation of the medial frontal cortex (MFC) and the parietal regions results from conflict monitoring, regardless of the type of stimulus. However, the specific contribution of different brain regions to conflict monitoring remains a subject of study. A recent work showed that dorsolateral prefrontal cortex (DLPFC) activity increases when inhibitory control is exercised (Hare et al., 2009). This result had already been found in previous studies, namely those that showed the activation of Brodmann Area (BA) 9 (Garavan, et al., 2002; Kübler et al., 2006; Liu et al., 2000; Liu, et al., 2004; Rubia et al., 2003), and BA 46 (Kübler, et al., 2006; Liu, et al., 2000, 2004). The inferior prefrontal cortex (IFC; BA 44) has also been associated to inhibitory (Garavan, et al., 2002; Wang et al., 2010).

Judging from evidence obtained with the Stroop and Simon tasks, areas of the anterior cingulate cortex (ACC) are activated in addition to the DLPFC when these tasks were performed (Banich et al., 2000a; Banich et al., 2000b; Leung et al., 2000; Milham et al., 2003; Milham et al., 2001; Milham et al., 2002), indicating attentional control (for a review, see Liu, et al., 2004). Although the specific role of the ACC areas is still unclear, attentional control has been associated with BAs 24 and 32 (MacDonald 3rd et al., 2000; Mansouri et al., 2009; Ridderinkhof et al., 2004), as well as with BA 6 of the posterior cingulated cortex (Garavan et al., 2002, Liu et al., 2004). In Garavan's study with the modified Go/No-Go task (Garavan et al., 2002), successful inhibition was associated with the right DLPC (BAs 9/44), the right inferior parietal lobule, and the ACC (BA32). Unsuccessful inhibition was associated with left BA 9, the more posterior region of the cingulate cortex (BAs 24/6), and other areas outside the focus of the present study.

An alternative to the paradigms mentioned above may be the Williams Inhibition Test (WIT). Combining the properties of the Stroop effect with those of the other instruments traditionally used in the assessment of executive functioning, such as the Wisconsin Card Sorting Test (WCST, Berg, 1948), the Williams Inhibition Test (WIT, Williams, 1992) is particularly interesting to the investigation and evaluation of executive functions. The WIT requires that the subject responds to a stimulus while inhibiting the response to competing stimuli, solves different problems and formulates rules that regulate behavior in the face of new circumstances. This makes the WIT a relatively simple non-verbal task that allows the assessment of cognitive flexibility and self-control (Martelli, 2005). However, its use is quite rare, and there is no evidence from neuroimaging of the activated areas during its performance.

The study of neural correlates of cognitive functions elicited by neuropsychological tests represents the intersection between neuroscience and cognitive psychology, and the combined use of different research methodologies, including biological and behavioral approaches, allows us to assess how brain regulations may relate to cognitive processes (Cabeza et al., 2005). Our study follows in this line of research, investigating the relationship between the cognitive functions thought to be elicited by the WIT, namely attention and inhibitory control, and brain areas that the literature identifies as being associated with these functions.

Considering the existing literature, we expect to obtain an increase in the BOLD signal in the DLPFC (BA 9/46), the IFC (BA 44), the ACC (BA 32) and the PCC (BA 6) associated with the implementation of the WIT. We also expect that the level of behavioral performance in the tasks under study is significantly lower in a group of people with brain injury than in healthy subjects. If these two predictions receive confirmation, we have the demonstration that the WIT can work as a paradigm for testing inhibitory control and attention, and that it discriminates situations of brain injury.

2. Material and methods

2.1 Study 1: Within-group neuroimaging and behavioral data

2.1.1 Participants

Ten right-handed, healthy participants (four males, six females, $M = 27.10$ years old, $SD = 2.89$) were recruited from the local community. All participants had normal or corrected to normal vision. They gave written informed consent before participating in this study. None of the participants had contraindication for MRI, or pathologies of the Central Nervous System (CNS), psychiatric disorders, or trauma.

2.1.2 Stimuli

The stimuli were the 60 trials which compose the WIT. Different types of distracters (plain circles, numbers, letters, colors, patterns, figures) are displayed for each stimulus (Williams, 2002). The level of difficulty associated with these distracters is the same for each block of 10 stimuli and increases for every new block of 10 stimuli. The stimulation protocol was prepared in SuperLab 4.5 (2011, Cedrus Co., California).

2.1.3 Design and Procedures

This experiment consisted of a single session of fMRI scanning during which participants observed the 60 stimuli of the WIT, repeated in three blocks. The whole session consisted of 180 trials, synchronized with the fMRI scans. Participants were instructed to always select the circle at the bottom that is of the same size as the circle on top. They should press the left (blue), right (red) or center (green) button, corresponding to the position of the circle chosen. A block design was used, with three cycles of rest and three cycles of activation each. Each block had a length of 150000 ms (2500 ms * 60 trials), plus 15000 ms for the resting cycle, during which participants were told to rest while paying attention to a fixation point. Participants were allowed to respond during the exhibition of each stimulus (i.e., 2500 ms). Behavioral data (accuracy and reaction times) and brain activation patterns were analyzed.

2.1.4 Acquisition

The MR scanning was carried out using a 3T scanner (MAGNETON Trio Tim 3T, Siemens), located at the Portugal Brain Imaging Network (BIN/ANIFC). It was equipped for echo-planar imaging (EPI) used for data acquisition.

Stimuli were presented using a high-resolution rear projection system (projector Avotec Silent Vision 6011) with responses recorded via a fiber-optics response pad with three buttons (Lumina MRI Pad, model LP-400, from Cambridge Research Systems, Ltd.). A laptop computer running SuperLab 4.5 controlled stimulus presentation and the recording of responses. Also, the timing of the stimulus presentation was synchronized with the magnet trigger pulses.

The study protocol consisted in the acquisition of a volumetric sequence of high resolution T1-weighted (TR = 2300 ms, TE = 2.98 ms, TI = 900 ms, 160 slices were obtained in a matrix of 256 mm with a voxel size of 1 x 1 x 1 mm, acquisition time 7 min 58 s), followed by the acquisition of functional data, using an EPI sequence (echo-planar imaging) 2D whole-brain (TR = 2500 ms, TE = 37 ms, matrix 104 x 104, voxel size of 2.5 x 2.5 x 2.5 mm, 210 volumes).

2.1.5 Image Analysis

Data preprocessing was performed using the software BrainVoyager QX 2.3 (2011, BrainInnovation, Netherlands). Preprocessing of functional data included slice time correction, 3D motion correction, spatial smoothing and temporal filtering. Functional and anatomical scans of the data were co-registered and normalized to Talairach space. A GLM-based random effects analysis was run on the data. Activation maps (thresholded at p-value < 0.001, uncorrected) were projected on standard Talairach Brain, where clusters on Brodmann areas related to the DLPC, (including BA 9, BA 44 and BA 46), ACC (BA 32) and PCC (BA 6) were identified.

2.2 Study 2: Between-Group Behavioral data

2.2.1 Participants

In this study, one stroke and seven Traumatic Brain Injury patients (Acquired Brain Injury group), 7 males and 1 female ($M = 28.80$ years old, $SD = 8.81$) were recruited from one rehabilitation institution in order for their performance to be compared with the data previously obtained with healthy participants. All of them had normal or corrected vision and did not have any motor disability that could interfere with performance. They gave written informed consent before taking part in this study.

2.2.2 Stimuli

See section 2.1.2 above.

2.2.3 Design and Procedures

The stimulation protocol was exactly the same as in Study 1 without the fMRI, as altered brains would not provide useful normative data about the areas being activated by the WIT task. In this group, the stimuli were presented on a laptop computer running Windows XP (2002, Microsoft), placed in front of the subjects. They responded by pressing keys one, two or three.

A comparative analysis of the two groups was conducted with the nonparametric Mann-Whitney U test in order to inspect whether the WIT task enables us to discriminate between healthy participants and individuals with probable attention and inhibitory deficits. Statistical analyses were performed in SPSS 18.0.

3. Results

3.1 Imaging Data

Task-related BOLD responses during the WIT condition for the selected regions of interest (ROIs) are presented in Table 1, complemented with Figure 1. Surface coloring represents the different brain areas that were activated during the WIT, as revealed by BA analysis.

Table 1 - *Brain areas activated during the WIT, as revealed by BA analysis.*

		TAL Coordinates				
BA	x *M (SD)*	*y M (SD)*	*z M (SD)*	*No. of Voxels*	*Average t*	*Average p*
BA6L	-33.82 (19.88)	3,18 (6.50)	33.51(13.53)	5129	6.188985	0.000260
BA9L	-40.91 (2.02)	25,53 (5.21)	31.37 (4.23)	615	5.727831	0.000311
BA32L	-5.31 (1.54)	-2.7 (4.35)	46.78 (3.36)	156	5.619362	0.000337
BA44L	-40.18 (5.58)	21.26 (10.31)	21,32 (7.57)	2082	5.426090	0.000414
BA46L	-35,8 (3.05)	38 (3.43)	21.78 (3.04)	403	5.497705	0.000428
BA6R	27,14 (18.10)	5,84 (6.10)	41.93 (10.29)	1700	5.782752	0.000342
BA44R	40,73 (5.94)	19,63 (9.31)	26.74 (6.22)	1300	5.466414	0.000435

Note. BA = Brodmann area

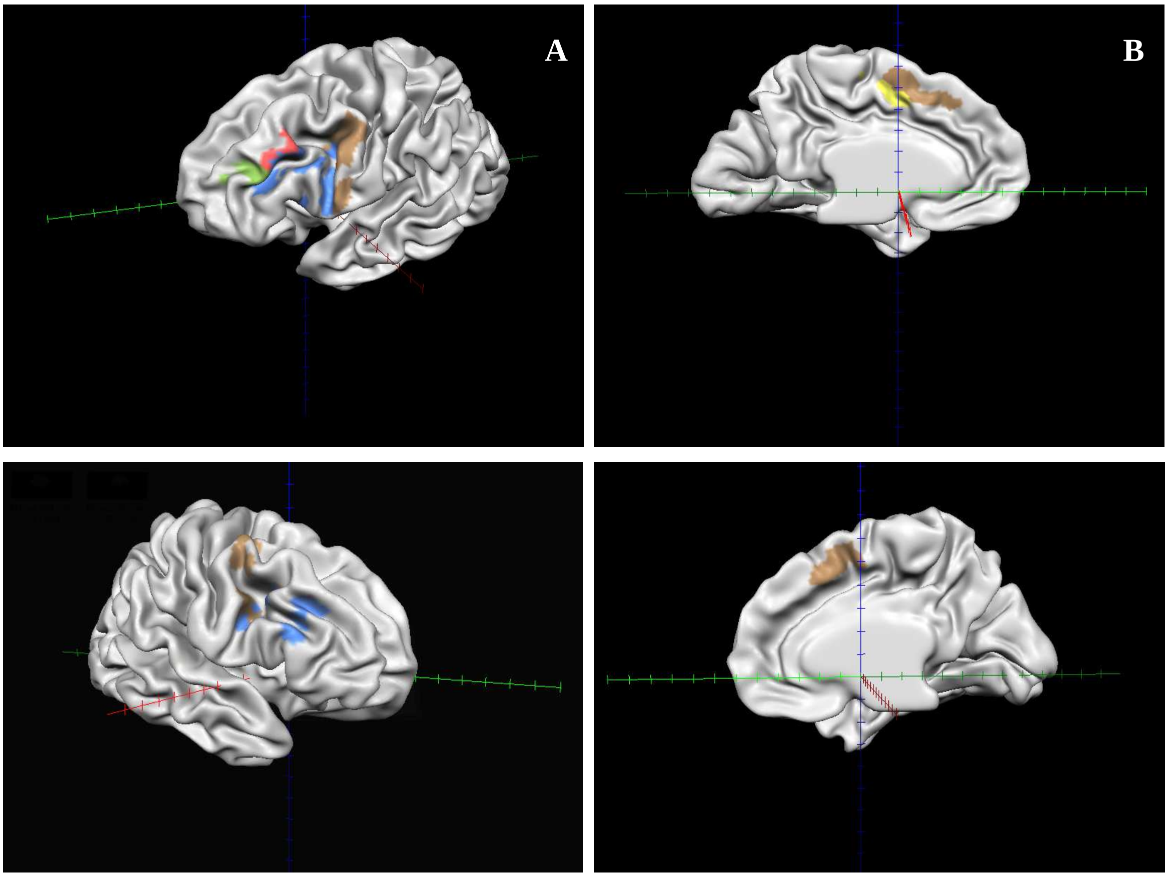

Figure 1. Top - Activations in the brain's left hemisphere revealed by BA analysis; Down - Activations in the brain's right hemisphere revealed by BA analysis (A. lateral view, B. medial view). Surface coloring represents the different BAs: brown = BA 6, red = BA 9, yellow = BA 32, blue = BA44, and green = BA 46.

3.2 Behavioral Data

Subject one of the healthy group was removed from the analysis of behavioral performance and of the Mann-Whitney test, because his were extreme values, by defect on hits and by excess on false alarms, suggesting that he responded randomly. Subject 15 of the ABI group was maintained, because although he also shows extreme values, this is not an unexpected result in brain injury participants.

Descriptive statistics for the behavioral performance on the WIT task of the two groups are presented in Table 2 and Figures 2 and 3.

Table 2 - Behavioral Performance *on the WIT task for the healthy and the ABI groups.*

	Group			
	Healthy		ABI	
	Mdn	*Range*	*Mdn*	*Range*
Hits	55.3	48.7-57.7	44.3	27.7-57.7
Errors				
Self-Corrected Responses	2.7	2.3-7.3	1.2	0.0-4.3
False Alarms	0.7	0.0-3.3	4.3	1.7-23.3
Omissions	0.0	0.0-0.3	5.2	0.3-22.0
Reaction Time	884	566-1221	2152	1703-2358

The Mann-Whitney test shows significant differences between the two groups for different types of errors and reaction times, and marginally significant differences for *hits* ($U(16) = 16.5$, $p = .06$). The ABI group has significantly more *false alarms* ($U(16) = 4.0$, $p = .002$), more *omissions* ($U(16) = 1.5$, $p = .001$), larger *reaction times* ($U(16) = 0.0$, $p = .001$) and less *self-corrected responses* ($U(16) = 10.5$, $p = .013$).

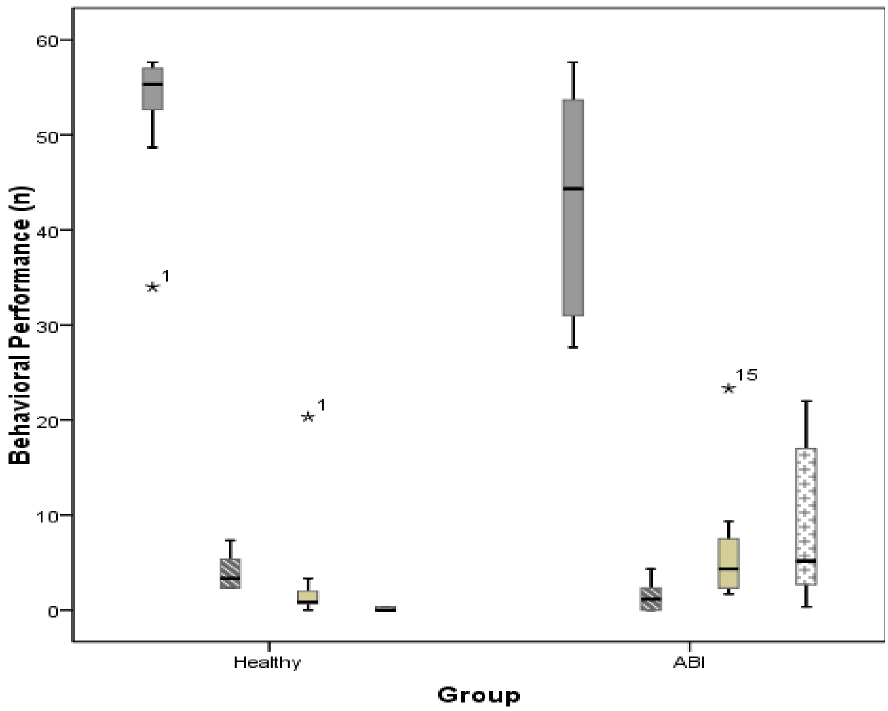

Figure 2. Behavioral performance (hits and errors – self-corrected responses, false alarms and omissions) by group. The bars represent confidence intervals; extreme values are marked with "*"

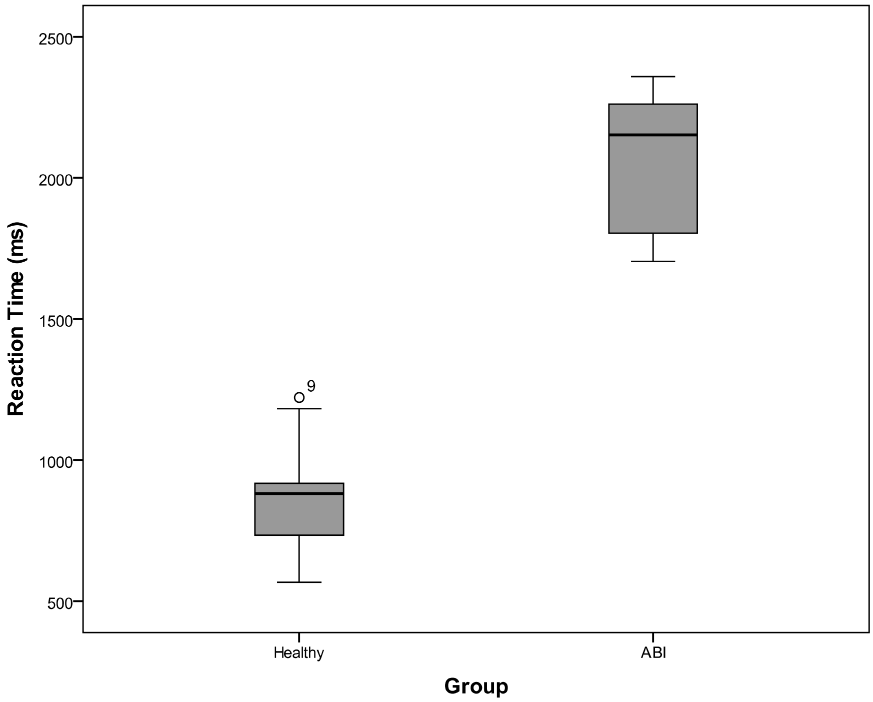

Figure 3. Behavioral performance (reaction times) by group. The bars represent confidence intervals; outliers are marked with "o".

4. Discussion

In this work we propose a new paradigm, based on the WIT, to study brain activation associated with attentional and inhibitory control. With this purpose, we analyzed both behavioral data (hits, errors and reaction times) in healthy and ABI subjects, and BOLD signals in healthy participants while performing the WIT.

The ROIs were theoretically defined based on previous imaging studies that analyzed the brain activation associated with attentional and inhibitory control. These earlier studies applied experimental paradigms based on Stroop, Simon or Go/No-Go tasks. In line with the literature reviewed we expected an increase in the BOLD signal in the DLPFC (BA 9/46), the IFC (BA 44), the ACC (BA 32) and the PCC (BA 6) associated with WIT performance. The analysis showed that all hypothesized regions are significantly activated while participants perform the WIT task.

The analysis of behavioral results shows a better performance in the healthy than in the ABI group, with a trend for an increased number of hits, fewer *false alarms* and *omissions*, shorter *reaction times*, and more s*elf-corrected responses* in healthy subjects. The latter result is expected, as it reflects the subjects' ability to correct an answer that they realize was incorrect. Consistent with these results, the fMRI data showed the activation of the ACC in the healthy group, considered involved in error detection and behavioral adjustment for subsequent trials.

The findings in the neuroimaging study are consistent with the results of previous works that identified the DLPFC, namely BA 9 (Garavan, et al., 2002; Kübler, et al., 2006; Liu, et al., 2000, 2004; Rubia, et al., 2003) and BA 46 (Kübler, et al., 2006; Liu, et al., 2000, 2004), the IFC (BA 44) (Garavan, et al., 2002; Menon et al., 2001), the ACC (BA 32) (MacDonald 3rd et al., 2000; Mansouri et al., 2009; Ridderinkhof et al., 2004) and the PCC (BA 6) (Garavan et al., 2002, Liu et al., 2004) as being involved in attentional and inhibitory control. Specifically, the DLPFC (BAs 9/46) is reported as having a role in inhibition and, more recently, in self-control (Hare et al., 2009). Also, theoretical literature indicates that, among other functions, BAs 6/9/46 are associated with executive control of behavior and BAs 32/44 are associated with cognitive and motor inhibition (Bernal and Perdomo, 2008). Research suggests that a typical task that activates the ACC is eliciting some form of conflict that can potentially result in error, as in the paradigm proposed here. Following the work of Milham and Banich (2005), several studies have sought to gather evidence about the contribution of this region. Neuroimaging studies of the Stroop task have assumed that the ACC has a critical role in the resolution of the Stroop interference condition. However, activation of the ACC seems to depend on a diversity of methodological factors, including the degree of response conflict and response expectancies. On the question of whether the task-conflict effect is actually processed in the ACC, in more dorsal regions of the MFC, or both, the present study reinforces the contribution of the ACC (BA 32), but we also observe an activation of the medial frontal gyrus (BA 6). These results are consistent with the results of, for example, Hazeltine et al. (2003), who also recognize the role of the MFC in conflict monitoring, regardless of the stimulus. BA44 activation has been identified in selective response suppression in Go/No-Go tasks and is suggested to assume a critical role in the suppression of response tendencies (Forstmann et al., 2008). This hypothesis can explain our results that also identify BOLD activation in this area. Unexpectedly, there seems to be a left-lateralized effect in this task that needs to be clarified in future studies.

5. Conclusion

This study shows the potential of the presented WIT-based block design paradigm in behavioral and neuroimaging studies of attentional and inhibitory control. It also reinforces the role of the DLPFC (BAs 9/46), the IFC (BA 44), the ACC (BA 32) and the PCC (BA 6) in these functions. Additionally, the behavioral results show that the WIT task seems sensitive to brain lesions, since it allows a good discrimination between healthy participants and individuals with brain injuries, even with a small sample.

The task proposed in this work differs from those typically reported in the literature in several ways: it is a non-verbal task, it is more demanding (i.e., distracters change, and the level of difficulty increases throughout the trials) and it is less known to the population. This last feature can be an advantage, because most studies use well-known Stroop, Simon or Go/No-Go tests, even if the extensive disclosure of a task could interfere with its validity.

Though future works should increase the size of the normative sample and introduce criteria validation through clinical groups, these findings can offer a valuable contribution to the study of attentional and inhibitory control, while providing a novel research paradigm for behavioral and neuroimaging studies.

Acknowledgments

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Artigo 11 - Study of Behavioral and Neural Bases of Visual Working Memory with an fMRI Paradigm Based on a Visuospatial N-Back Task

Dores, A. R., Barbosa, F., Carvalho, I. P., Almeida, I., Guerreiro, S. Martins da Rocha, B., de Sousa, L., & Castro Caldas A. (a submeter). Study of behavioral and neural bases of visual working memory with an fMRI paradigm based on a visuospatial n-back task.

Study of behavioral and neural bases of visual working memory with an fMRI paradigm based on a visuospatial n-back task

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Abstract

This study proposes and validates a new fMRI paradigm using a language-free adaptation of the 2-back working memory task in order to avoid cultural and educational bias. It also provides an index of the capacity of this experimental task to discriminate between healthy participants and individuals with minor working memory (WM) deficits. Ten healthy participants and 11 patients with acquired brain injury (ABI) performed an adapted 2-back WM task in a block design experiment with four runs and repeated trials. Data were analyzed with GLM-based random effects procedures and *t*-tests. Results show an increased BOLD signal in healthy participants, in a part of a network of distributed brain areas in the dorsal and ventral visual pathways engaged in visuospatial information processing (in the specialized areas for visual WM in particular). Concerning the capacity of this task to discriminate between healthy and ABI participants, behavioral data shows the predicted pattern of more hits, less omissions and a tendency for fewer false alarms, more self-corrected responses and faster reaction times in healthy participants, compared with moderate ABI patients showing low-average Working Memory Index (WMI). The results suggest that this non-verbal WM task can be used as a research methodology for behavioral and neuroimaging studies of visual WM in block-design paradigms. In addition to providing exploratory normative data, this study also introduces a validation criterion through a clinical group.

Keywords: *Block-design Visuospatial Working Memory Task*; Working memory; functional Magnetic Resonance Imaging (fMRI); Behavioral performance.

1. Introduction[17]

Working memory (WM) refers to storing information in a temporary system that allows monitoring and manipulating information in a relevant way to a current task, such as solving a problem. It also seems to be involved in other cognitive functions, such as reasoning and spatial processing.

Like memory function itself, which is considered a system of dissociable processes, WM is not a unitary system. Different neuroimaging studies have identified greater involvement of certain brain regions than others in this cognitive function. However, consideration for the participation in various degrees of each of the different regions involved is usually advocated in today's study of the neural substrates of WM (Haxby, Petit, Ungerleider, & Courtney, 2000). This cognitive function is mediated by a distributed neural system of several bilateral anterior and posterior regions of the cortex (Cabeza & Nyberg, 2000), specifically, the lateral and medial prefrontal cortex, anterior cingulate, posterior parietal, and occipital regions (Cicerone, 2002).

The literature in the field contains hundreds of neuroimage studies focusing on the tasks that can be used to examine the neural substrates of working memory processes. These studies use different tasks (n-back tasks are among them) with either verbal (digits, letters, or words) or non-verbal (e.g. spatial locations, colors, abstract objects, faces) stimuli (Cabeza & Nyberg, 2000; D'Esposito, et al., 1998; Owen, 1997). Most of the tasks employed to study visual WM have been derived from the procedure of Luck and Vogel (1997). Results indicate that different neural areas are involved in WM according to the tasks. For example, in a visuospatial n-back task with two memory-load conditions (0-back, 1-back, 2-back), Carlson and colleagues (1998) found that a network of distributed brain areas in the dorsal visual pathway was activated when the memory load was higher. Specifically, a bilateral activation of the medial frontal gyrus (MFG), the superior frontal sulcus and adjacent areas (SFS/SFG), as well as the intraparietal sulcus (IPS), was observed in most participants. An activation in the inferior frontal gyrus, in the medial superior frontal gyrus, precentral gyrus, superior and inferior parietal lobuli, occipital visual association areas, anterior and posterior cingulate areas, and insula was also found (Carlson et al., 1998).

Not surprisingly, despite the variation in the neural pathways with the different tasks, a common substrate to all of them has also been identified in the study of WM. That is the case of the dorsal (BAs 9, 46, 9/46) and ventral (BAs 45, 47) regions of the

[17] As referências bibliográficas deste artigo encontram-se no formato proposto pela revista a que foi submetido.

prefrontal cortex, even if this subdivision of the PFC is becoming to be considered coarse (D'Esposito, 2008; Postle & D'Esposito, 2000).

In what concerns the contribution of the parietal lobe (for a review, see Berryhill, Chein, & Olson, 2011; Berryhill & Olson, 2008a, 2008b), its superior portion (SPL; BA 5 and 7) is recognized as being involved in spatial WM (Olson & Berryhill, 2009; Wager & Smith, 2003). Regions near the intraparietal sulcus and more inferior portions of the posterior parietal cortex (PPC), particularly in the right hemisphere, seem to have a significant role in the WM of objects (Todd & Marois, 2005). The role of the medial temporal lobe has also been recognized (Olson & Ezzyat, 2008), because when lesions of this brain region occur, visual WM is also impaired (Olson, Moore, Stark, & Chatterjee, 2006).

This diversity in WM models and in studies' results may be partly due to the methodologies and paradigms used. The n-back WM tasks used in many studies are dependent on language (as their items are numbers or letters), possibly leading to outcomes that may reflect cultural and educational biases. They invoke verbal WM processes that can mask other WM processes, such as the visuospatial ones. If language is impaired, as is often the case in acquired brain injury (ABI) patients, disentangling the above-mentioned processes may be particularly important for both research and clinical purposes. Language-free tasks contribute to a broader understanding of WM in general and are particularly useful in cases of brain injury. The paradigm in this study was inspired in existing stimulus material for visuospatial WM research (Hautzel, et al., 2002; Owen, McMillan, Laird, & Bullmore, 2005), which was adapted for an fMRI block-design protocol. In fact, although we are only focused on the WM task in this paper, the stimulation paradigm also comprises a sustained attention task employing the same stimuli. The final purpose was to prepare attention and WM tasks for fMRI using non-verbal, and coherent stimuli in such a way that they would be easily understood and performed by mild to moderate ABI patients, either for research or clinical applications.

In this work we report behavioral and fMRI data concerning the WM task to show that it can be used with the intended purpose. The paradigm uses a language-free adaptation of the 2-back WM task in order to avoid language impairments, as well as cultural and educational bias – the *Block-design Visual Working Memory Task for fMRI* (Barbosa, et al., 2010). Based on the literature, this study aims to test if the proposed paradigm produces an increase of the BOLD signal in specialized areas related with visual WM areas in healthy participants. Another objective for this study is to assess whether this fMRI task allows good discrimination between healthy participants and brain injured patients, by checking if healthy subjects perform it better than a group of individuals with moderate ABI showing minor WM deficits in neuropsychological evaluations. By using such a group of patients, with no severe brain injuries or WM impairments, we sought to obtain better data on the discriminative properties of the task. In other words, we explored the validity of this experimental task to the study and evaluation of visuospatial WM processes and its capacity to discriminate between healthy participants and ABI individuals with minor WM deficits by testing the hypotheses that (a) the neurobiological correlates of this task are equivalent to those found in the literature on the neuroanatomical bases of visual WM, and that (b) the performance in this task is lower in the ABI group, even if this last group does not show substantial WM deficits in conventional neuropsychological measures.

2. Material and methods

2.1 Study 1: Within-group neuroimaging and behavioral data

2.1.1 Participants

Ten right-handed healthy participants, with a mean of *27.10* years old (*SD = 2.*89) and a mean education level of 11.4 years (*SD* = 2.3), were recruited from the local community. Six were male and four were female. All participants had normal or corrected to normal vision. None had contraindications for MRI, or pathologies of the Central Nervous System (CNS), psychiatric disorders, or trauma. All gave written informed consent before participating in this study.

2.1.2 Stimuli

The stimuli consisted of nine-square matrices with one of the squares painted in black. Thirty-six stimuli were presented were presented using a high-resolution rear projection system (Avotec Silent Vision 6011 projector) with responses recorded via a fiber-optics response pad (Lumina Response Pad for fMRI, LU400-Pair model, Cedrus Corporation). The stimulation protocol was prepared in SuperLab 4.5 (2011, Cedrus Co., California), and a laptop computer running the same software was used to control stimuli presentation and to record the responses.

2.1.3 Design and Procedures

This experiment was organized according to a block design paradigm in a single session of fMRI scanning during which participants observed the 36 stimuli of the Block-*design Visual Working Memory Task for fMRI* (Figure 1), repeated in four cycles. Each cycle consisted of a resting period of 15000 ms, immediately followed by an activation block in which the 36 stimuli were presented, one at a time (650 ms of exposure time), with an inter-stimuli interval (ISI) of 2350 ms (corresponding to a total of 3000 ms per trial). Twelve of each 36 stimuli were targets (33%), following usual proportions for this task, presented in a pseudorandom order to avoid more than two consecutive targets or equal stimuli. Both blocks were synchronized with the fMRI scans.

Participants were instructed to pay attention to a sequence of visual stimuli and press a pre-defined button, as fast as possible, when detecting a target, i.e. each time the black square was the same as the one two trials back. During the resting cycles participants were told to rest while paying attention to a fixation point. Participants were allowed to respond during the exhibition of each stimulus.

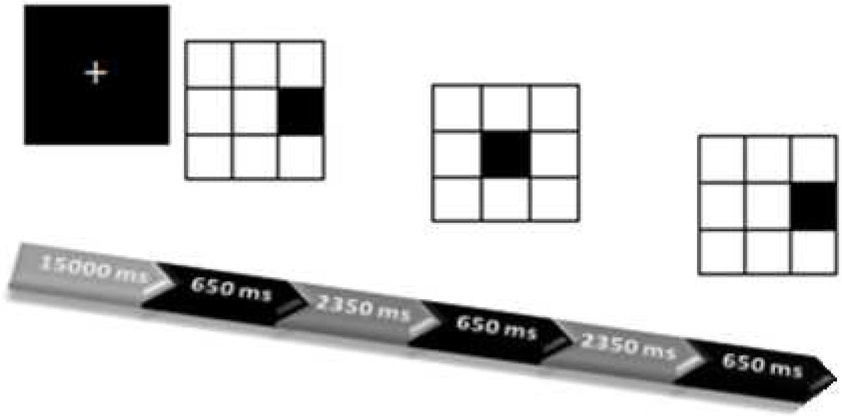

Figure 1. Block-design Visual Working Memory Task for fMRI. The sequence represents: resting period, exposure time and inter-stimuli interval. The third nine-square matrix represents a target-stimulus.

2.1.4 Acquisition

The MR scanning was carried out using a 3T scanner (MAGNETON Trio Tim (Total Imaging Matrix) 3T, Siemens), located at the Portugal Brain Imaging Network (BIN/ANIFC). It was equipped for echo-planar imaging (EPI) used for data acquisition. The timing of the stimulus presentation was synchronized with the magnet trigger pulses.

The study protocol consisted in the acquisition of a of T1-6t high resolution volumetric sequence (TR = 2300 ms, TE = 2.98 ms, TI = 900 ms; 160 slices were obtained in a matrix of 256 mm with a voxel size of 1 x 1 x 1 mm), followed by the acquisition of functional data, using an EPI sequence (echo-planar imaging) 2D whole-brain analysis (TR = 2500 ms, TE = 37 ms, matrix 104 x 104, voxel size of 2.5 x 2.5 x 3 mm).

2.1.5 Data Analysis

Data preprocessing was performed using the BrainVoyager QX 2.3 software (2011, Brain Innovation, The Netherlands). Preprocessing of functional data included slice time correction, 3D motion correction, spatial smoothing and temporal filtering. Functional and anatomical scans of the data were co-registered and normalized to Talairach space. Activation during the 2-back task was contrasted against the observation of the fixation point. A GLM-based random effects analysis was run on the data. A whole brain analysis focusing on Brodmann's areas was performed through activation maps (with the threshold at p-value < 0.001, for correcting for multiple comparisons) excluding activation areas with less than 300 voxels.

2.2 Study 2: Between-Group Behavioral data

2.2.1 Participants

In this second study, nine ABI participants (7 males, 2 females), five stroke and four Traumatic Brain Injury (TBI) patients, with a mean of 29.7 years old (*SD* = 4.8) and a mean education level of 9.7 years (*SD* = 3.9), were recruited from one rehabilitation institution in order for their performance to be compared with the data previously obtained with healthy participants. Although the causes of brain injury were variable, there were no severe brain injury patients in the group, as they could not attend to the Rehabilitation Program offered by the institution from where participants were recruited. All of them had normal or corrected to normal vision and no motor disability that could interfere with their performance. They gave their written informed consent before taking part in this study.

2.2.2 Stimuli

See section 2.1.2 above.

2.2.3 Design and Procedures

The WM of the ABI participants was previously tested with the Wechsler Memory Scale III – Third Edition (WMS-III, Wechsler, 2008), in order to compute the Working Memory Index (WMI), and a low-average score was obtained (*M* = 85.0; *SD* = 15). The stimulation protocol and procedures were exactly the same as in Study 1. The fMRI results of this group are not presented, though, as altered brains would not provide useful normative data about the areas being activated by the *Block-design Visual Working Memory Task for fMRI* (Barbosa et al., 2010).

2.2.4 *Data Analysis*

Behavioral data (accuracy and reaction times) were analyzed. A comparative analysis of the two groups was conducted on behavioral data with *t*-tests. Statistical analyses were performed in SPSS 18.0.

3. Results

3.1 Imaging Data

Task-related BOLD responses for the whole brain in healthy participants during the *Block-design Visual Working Memory Task for fMRI* are presented in Table 1 and complemented with Figure 2.

Table 1
Brain areas activated during the Block-design Visual Working Memory Task for fMRI, *as revealed by whole brain BA analysis in healthy participants.*

BA	x *M(SD)*	*y M (SD)*	*z M (SD)*	*No. of Voxels*	*Average t*	*Average p*
BA4L	-36.00 (8.00)	-7.67 (3.00)	50.22 (5.30)	1241	11.700.088	0.000001
BA6L	-31.31 (18.93)	4.48 (7.53)	37.22 (10.21)	3545	7.733.869	0.000029
BA7L	-28.21 (11.91)	-58.12 (10.82)	42.99 (4.54)	4316	9.238.437	0.000007
BA9L	-40.30 (2.34)	22.56 (4.37)	34.62 (3.80)	925	7.909.834	0.000024
BA17L	-14.11 (8.46)	-90.17 (5.91)	1.01 (8.15)	1002	5.632.151	0.000321
BA18L	-22.85 (10.51)	-79.81 (4.269)	4.44 (15.98)	573	9.167.931	0.000007
BA39L	-49.05 (3.29)	-49.83 (2.94)	35.44 (4.90)	576	7.501.182	0.000037
BA44L	-40.39 (4.52)	13.37 (9.05)	27.26 (6.56)	853	7.111.234	0.000056
BA45L	-33.04 (2.32)	20.21 (3.54)	8.48 (2.99)	344	6.620.371	0.000097
BA47L	-31.86 (2.93)	19.78 (2.98)	5.01 (2.65)	376	5.937.047	0.000219
BA4R	22.80 (7.78)	-6.33 (4.50)	51.30 (2.77)	1179	8.086.189	0.000020
BA6R	27.16 (17.97)	9.03 (7.57)	40.41 (8.37)	3032	10.483.876	0.000002
BA7R	25.43 (13.02)	-58.05 (12.14)	44.69 (5.58)	3583	10.565.937	0.000002
BA9R	37.78 (3.73)	30.38 (7.11)	36.38 (3.46)	706	6.527.842	0.000108
BA17R	12.70 (11.79)	-86.99 (4.43)	0.98 (8.88)	818	6.257.608	0.000148
BA18R	30.95 (5.39)	-77.75 (2.83)	15.66 (10.22)	907	6.659.940	0.000093
BA19R	30.44 (7.22)	-63.81 (7.94)	33.45 (15.37)	3309	8.018.610	0.000022
BA44R	40.50 (5.37)	18.66 (10.17)	30.54 (5.76)	1295	6.689.806	0.000090
BA46R	31.85 (3.04)	51.42 (3.89)	19.63 (4.34)	477	5.502.589	0.000379

BA47R	30.42 (2.51)	21.58 (2.81)	3.53 (3.83)	555	5.561.234	0.000351

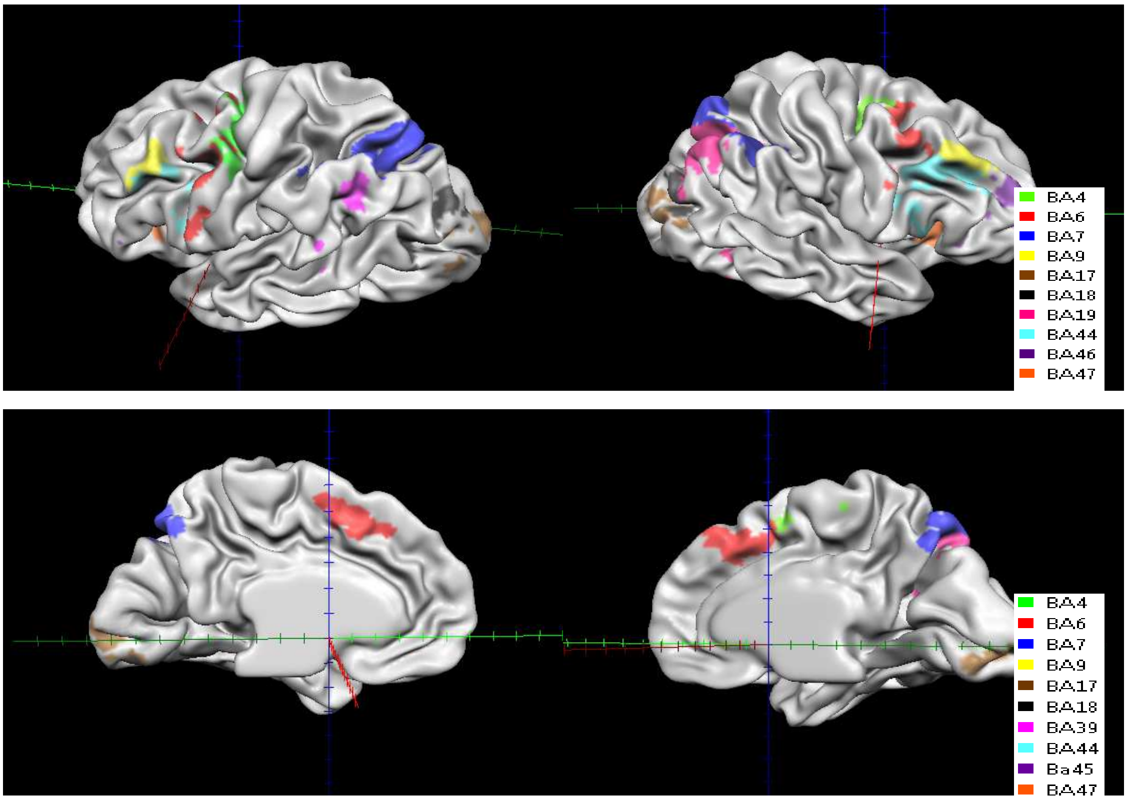

Figure 2. Activations in the brain's left hemisphere (left) and right hemisphere (right) revealed by BA analysis for healthy participants. Surface coloring represents the different BAs (top - lateral views; down - medial views).

3.2 Behavioral Data

Descriptive statistics for behavioral performances on the *Block-design Visual Working Memory Task for fMRI* of the healthy and the ABI groups are presented in Table 2.

Table 2. - Behavioral Performance (Mean and Standard Deviation) *on the* Block-design Visuospatial Working Memory Task *for fMRI of the healthy and the ABI groups.*

	Group	
Behavioral Performance	Healthy M (SD)	ABI M(SD)
Hits	31.0 (10.6)	18.2 (10.1)
Errors		
Omissions	16.9 (10.6)	31.4 (9.0)
False Alarms	0.6 (0.1)	6.0 (7.4)
Self-Corrected Responses	3.0 (1.2)	1.8 (1.1)

Reaction Times	442 (50.3)	483 (51.6)

The *t*-test reveals a group effect for Errors. Specifically, compared with the healthy participants, the ABI group shows more omissions (t(28) = 3.9, p = .001), and false alarms (t(28) = 2.3, p = .03). Likewise, ABI group shows significantly less hits (t(28) = -3.2, p = .003), and less self-corrected responses (t(28) = -2.8, p = .008). Finally, we also found a group effect for reaction times, with the ABI participants displaying longer latencies than controls (t(28) = 2.1, p = .048).

4. Discussion

The present work analyzed BOLD signals in healthy participants and behavioral data (hits, errors and reaction times) in healthy and in ABI subjects while performing the *Block-design Visuospatial Working Memory Task* (Barbosa et al., 2010) proposed in our work.

As expected, we found higher activation of brain regions associated with specialized areas for spatial WM (Superior Frontal Sulcus, BA 6, but not BA8). We found increased activation in DLPC (BA 9/46) which is considered to be the "locus" of active manipulation of information, as well as in the bilateral ventrolateral prefrontal cortex (BA 47, inferior frontal gyrus pars orbitalis), considered to be involved in maintaining the information (D'Esposito, et al., 1998), show increased activation. The inferior frontal gyrus (BAs 44/45), as well as the premotor cortex (bilateral BA 6), reported in the literature as associated with performance of n-back tasks (see, for example, Carlson, et al., 1998) are also activated in this study. The same occurs with bilateral activations of BA 4 (primary motor cortex – precentral gyrus). This is not surprising given that performance of the *Block-design Visuospatial Working Memory Task* requires motor responses. Similar activations were reported in other studies (Metzak et al., 2011; Ventre-Dominey et al., 2005).

We found a lateralized prefrontal activation in the activation of the right lateral prefrontal region which has been previously associated with visuospatial processing (Baddeley, 1995; Baddeley & Hitch, 1974) was also observed here. However, a large region of the left prefrontal cortex (BAs 4/6/7/9/44/45/47) was also involved. Thus, these PFC regions seem to subserve spatial working memory, as recent literature suggests (Bor, Duncan, Wiseman, & Owen, 2003; Manoach, et al., 2004). Considering that the bilateral PFC activation might alternatively result from an involvement of central executive subfunctions and therefore stimulus-independent, in future studies we must consider also other tasks because the n-back does not discriminate well these subprocesses.

The right inferior parietal cortex (BA 40) that Baddeley (2003) considers the brain area corresponding to the visuospatial sketchpad and the inferred area of the storage constituent of the loop was not sufficiently activated in our task. However, some studies reporting the activation of BA 40 also report the activation in right BAs 6/47/19, and these same areas were also identified in our study (Baddeley, 2003; Smith, Jonides, & Koeppe, 1996). Consistent with the findings of Rämä and colleagues (2001), the inferior parietal lobe (BAs 7/19/39) and the intraparietal sulcus (BA 7, but not BA 40) were activated, as well as visual association areas, including the lingual and fusiform gyri (BA 17/18). Finally, and as previously reported in the literature, we found evidence that several bilateral anterior and posterior regions of the cortex are involved, indicating that a distributed neural system is implicated in WM (Cabeza & Nyberg, 2000; Cicerone, 2002). So, despite the emphasis on prefrontal regions, a network of distributed brain areas, with the involvement of subregions of the prefrontal, parietal, and occipital regions, consistent with the emerging literature, was shown.

Concerning the behavior measures, a brief analysis of the error-types and reaction times suggests that ABI participants were committed to the task. More precisely, an increased number of false alarms together with larger reaction times, as well as a number of hits above chance, denote that participants are trying to respond and they are not doing it impulsively. That said, further analysis shows that the healthy group displayed the predicted pattern of more hits, less omissions and fewer false alarms, more self-corrected responses and faster reaction times, when compared with ABI subjects with low-average WM. These difficulties in behavioral accuracy and the decrease in processing speed are common consequences of brain injury and have been extensively shown in the literature (Johansson & Tornmalm, 2012).

The activation in the primary visual cortex and the motor activation may be due to the different in- and output of the two contrasted conditions, therefore not directly attributable to WM processes. The n-back task will be shortly compared against the attention task in order to overcome this shortcoming. The current study introduces criteria validation for this specific task through a clinical group, and provides some exploratory normative data. Although larger samples are necessary for the purpose of generating sound normative data, this research paradigm for combined behavioral and neuroimaging studies, and the results we are presenting, will hopefully offer a useful contribution to the study of visual working memory.

5. Conclusion

WM has traditionally been investigated with tasks such as the maintenance of words, letters and digits, i.e. verbal stimuli, or even colors or faces, i.e., non-verbal stimuli. The non-verbal WM task proposed here minimizes shortcomings resulting from language impairments, as well as from cultural and educational biases, that could mask actual WM difficulties and their neural correlates. Although the type of material used is inspired in other visuospatial tasks, this task was prepared for a block-design fMRI paradigm, which was designed to be administered to patients with ABI, together with a sustained attention task, employing the same stimulus material (which facilitates the understanding of the task and the process of instructing participants). While administering these tasks, we also noticed that using nine-square matrices with one of the squares painted black may also allow screening out impairments in visual fields, which is an interesting side advantage, but further studies are necessary on this matter. For now, our results suggest that this block-design paradigm is valid for inducing WM processes, and can be used as a basic or clinical research methodology for behavioral and neuroimaging studies. This study also supports the advantages of combining multiple assessment tools (i.e., behavioral and neurophysiological measures) while analyzing mental processes or the means to induce them.

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IV. Trabalhos em Curso

Artigo 12 – Virtual City: Neurocognitive Rehabilitation of Acquired Brain Injury

Dores, A. R., Miranda, M. J. Carvalho, I. P., Mendes, L., Barbosa, F., Coelho, A., de Sousa, L., & Castro Caldas, A. (submetido). Virtual City: Neurocognitive Rehabilitation of Acquired Brain Injury. SGaMePlay 2012 - Second Iberian Workshop on Serious Games and Meaningful Play and 7th CISTI - Iberian Conference on Information Systems and Technologies 20th Madrid, Spain.

Virtual City: Neurocognitive Rehabilitation of Acquired Brain Injury

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Abstract

Acquired Brain Injury (ABI) is one of the leading causes of individuals' reduced participation in various contexts of life, compromising autonomous functioning and performance in complex activities. Neurocognitive rehabilitation, carried out by transdisciplinary teams, is part of the intervention after the acute phase, aiming patients' maximum functionality and quality of life. Serious games and virtual reality begin to provide innovative solutions in this area. In this study, a prototype platform for the rehabilitation of executive functioning and other related cognitive functions is presented: the Virtual City. Part of a larger project, it consists of urban virtual environments that simulate real-life scenarios and activities. Tests will be performed to validate it as a tool for the rehabilitation of ABI.

Keywords: Serious games; Virtual reality; Neurocognitive ehabilitation; Acquired brain injury (ABI); Executive dysfunction.

Introduction[18]

The application of new technologies to health and rehabilitation has grown significantly in recent decades, with

good potential. Specifically in the context of neurocognitive rehabilitation, serious games (SG) and virtual reality (VR) have allowed the development of programs that complement or replace traditional practices. The proximity of the scenarios and activities to real-life environments helps to increase the potential for generalization of acquired skills and consequently to improve the participation of patients in various contexts of life.

In this paper we introduce SG and VR as promising and innovative technologies in the field of neurocognitive rehabilitation. We also describe and present the *Virtual City* gameplay, algorithm and architecture, under development as part of the *Computer-Assisted Rehabilitation Program – Virtual Reality (CARP-VR)*. This platform is an instance of SG, customized to the rehabilitation of executive functioning and related cognitive functions, such as visuospatial processing, attention and memory in adult patients with Acquired Brain Injury (ABI). Finally, we present future directions concerning the validation of the *Virtual City* as a tool for the rehabilitation of ABI.

Acquired Brain Injury

From Causes to Consequences

ABI remains the leading cause of death and disability in adults and children [1, 2]. Among the causes of death by brain injury are road traffic accidents (23%), suicide (17%), violence (11%) and falls (7%) [3]. The number of people who survive to these different conditions is significantly higher today as a result of the quality of emergency services. Anticipated human, social, psychological and economic consequences are then associated not only with deaths, but also with survivors who become temporarily or permanently disabled [4, 5]. The economic costs associated with treatment in the acute phase (e.g., emergency services) and with treatment of severe or moderate injuries and their consequences (e.g., neuropsychological and physical rehabilitation, home care, family support), represent an important percentage of the gross national product of different countries [1, 6].

The design, development and implementation of effective and innovative interventions that optimize the effects of neuropsychological rehabilitation in general and of neurocognitive rehabilitation in particular are thus crucial. Intensive rehabilitation

[18] As referências bibliográficas deste artigo encontram-se no formato proposto pela revista em que foi aceite. Foi publicado numa versão mais reduzida.

remains the most significant means by which ABI survivors optimize recovery, independently of the type of brain injury (i.e., focal or diffuse) and of its consequences (i.e., global dysfunction or predominantly cognitive-behavioral sequelae).

Rehabilitation's ultimate end is the promotion of patients' independence and quality of life, and the increase of their participation in life contexts (for a better understanding of neuropsychological rehabilitation, see [7]). Today, many studies show evidence of neuronal plasticity that support neurocognitive rehabilitation beyond the functional gains [8].

Innovative Solutions for Effective Health Interventions and Rehabilitation

Among the diversity of definitions, SG can be described as "a mental contest, played with a computer in accordance with specific rules, which uses entertainment to further government or corporate training, education, health, public policy, and strategic communication objectives." [9] or "Games that do not have entertainment, enjoyment or fun as their primary purpose." [10]. This field has continuously been growing in the last ten years. Positive results with SG implementation have been reported in several areas, including rehabilitation [11-13]. As expected, the characteristics of this technology help to overcome the difficulties associated with a rehabilitation process, which is often long, slow, costly and demanding. This includes the current trend to produce "kit-based" games that make it possible for therapists/clinicians to modify the games on their own, according to the patients' needs.

The same applies to VR. A literature review shows the diversity of developmental stages – children, adolescents, the elderly [14-16] – cognitive functions – attention, memory, executive functions, among others [17-19] – and diagnoses in which VR starts to be applied, often in combination with gaming technology. For example, VR has been applied to pain [20], motor rehabilitation [21], manipulation of wheel chairs [22], neurocognitive rehabilitation of people with traumatic brain injuries [4], or even victims of cardiovascular diseases [19], such as stroke [5]. In the field of mental health, VR has been applied to the treatment of phobias [23], post-traumatic stress disorders [24], addictive behavior and other impulse disorders [25]. Applications to panic disorders [26], eating disorders [27], Parkinson's disease [28], Down syndrome [29], Attention Deficit Hyperactivity Disorder, Autism, and Cerebral Palsy [30], are also known.

This technology's main characteristics of presence, involvement and interaction, among equally important others, such as customization, immediate feedback or "gaming" factors, contribute to its potential.

Despite VR and SG's advantages, as well as their preliminary positive results, further research on their effects is needed to examine and demonstrate, in a nonobjectionable way, the clinical effectiveness of these technologies compared to the traditional techniques.

Virtual city: Development

Game Description

Researchers and practitioners from diverse backgrounds are involved in this project, working on the design, development and implementation of CARP-VR as a new rehabilitation platform of which this work is a part. CARP-VR is an SG for neurocognitive rehabilitation of people with ABI. It consists of three-dimensional (3D) virtual environments that simulate real-life scenarios, i.e., a House and a Supermarket already in the implementation phase, and a Virtual City under development, presented here. In this CARP-VR, patients can perform different activities concerning daily situations (e.g., shopping, navigating in city streets on foot or by employing a sequence of different means of transportation, managing a planner, money, time, distances, and solving problems in general). Virtual City, gives access to the other scenarios (House and Supermarket) when, during the game, the user selects the respective buildings. The game is at once a new way of improving clinical recovery, evaluating patients' progress and transferring the acquired skills to daily life situations, as explained later. The combination of these features makes this an innovative platform, differentiating it from others that already exist.

Among the areas in which ABI patients show deficit, independent mobility using means of transportation needs special attention, because it is crucial to the integration of people with disabilities back in the community [31]. Some simple tasks, like crossing the street or calling a taxi, may be very complex for ABI patients.

However, this population's direct contact with reality is still limited during rehabilitation. Existing solutions do not allow the variety and frequency of individual participation that patients need and professionals consider acceptable [32]. The employment of self-instructional training to help the development of metacognitive strategies in cases of impulsivity, reduced capacity of planning, organizing, task-switching and problem-solving may be helpful [33]. However, much work is still necessary to provide motivating, safe, enjoyable, and logistically feasible activities that elicit the damaged cognitive function(s), contributing to their rehabilitation and/or to the (re)acquisition of competences. These are issues considered in the design and development of the Virtual City.

The development of CARP-VR: Virtual City begins with the program's general conceptual design. The psychologists' team members present the project's desiderata according to the specificities of the population to be studied (namely, activities to be performed in each environment, number of levels of difficulty for the activities, blocks and sessions) and engineers contribute suggestions for the computational operationalization of these desiderata. Then, the detailed conceptual design of each of the agreed components (Interaction Application and Virtual Environments) takes place. Finally, assessment instruments (usability, neuropsychological and functionality tests, and fMRI paradigms) to be applied before and after the intervention, for intra- and inter-subject, pre- and post-test evaluation will also be specified. In sum, the conceptual design is a continuous activity requiring constant literature review, expert consultation, and document/report writing.

The Virtual City is a first-person game intended to simulate a part of a portuguese city. It allows the development of patients' basic skills to perform tasks and to solve problems that are part of daily life, in a familiar environment.

The game starts in the user's virtual house. The first step in the user's real day is to plan; the second is to execute what was planned. During the game, the user will need to do the same: first to schedule the tasks and then to execute them. Each task has a description, a place, a level of relevance (very important, important, not important) and a limited period of time to be performed.

In order to reach the task's place, the user needs to move around the city on foot or using one of five vehicles: car, taxi, subway, train or bus. The main challenge is to complete all the tasks with the best solution, combining the fastest way and the least expensive vehicle, since all these vehicles have an associated cost and time, as in real life.

During all the game, the users will know how well they are doing, receiving frequent notifications about their performance. The system provides three types of feedback: the instantaneous and the periodic types are both automatic; the third type is required by the patient or by the therapist. Every time the user fails the current task, the system returns an instantaneous error message, using text and sound signals. At the end of the levels, blocks or sessions, the system provides a periodical brief report about the user's performance, showing the difference between the user's path and the initial path, the user's time and the minimum time and how many tasks were solved. Patients and therapists can also ask for extra information stored in the 'historic' menu, where it is possible to analyze the user's progress per level, block or session.

Gameplay

The game is divided in sessions, blocks and levels (Fig. 1). Every time a patient starts a new appointment, whether with a therapist or alone, a new session begins. A session can be closed and resumed later, upon date saving, for future evaluation. A new session starts at the level after the one that was previously completed. If the last level was not successfully finished, it must be repeated.

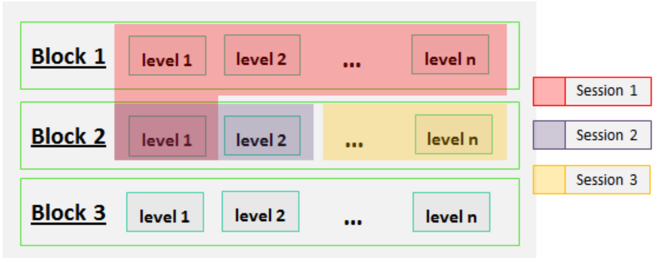

Figure 1 – Game Logic

The level is completed when the user passes its two phases: Planning and Performing (Fig. 2). First, patients receive tasks that are completely disorganized, and they need to distribute them on their daily planner. Then, patients need to perform the tasks in the same order as planned before, walking through the city via different vehicles. Task planning and performing are considered according to goals relevant for the rehabilitation of the cognitive functions affected, i.e., visuospatial, attention, memory, and executive functions, in a growing level of complexity. The game is thus divided in blocks, each focusing on a new ability on how to live in a real life (e.g., managing task importance, time, distance, money).

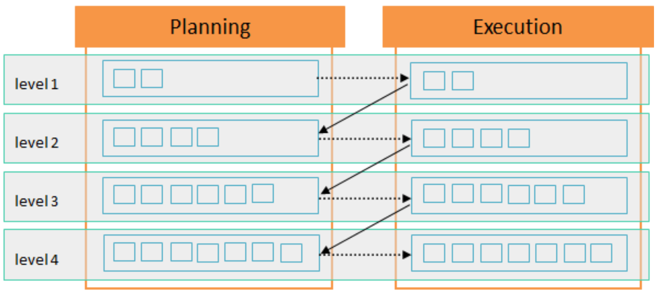

Figure 2- Levels' progress

A block consists of a set of levels sharing the same goals. The game has seven blocks with different points of training, but the goals are cumulative. The current block has always the goal from the previous block plus a new one, a new purpose of training. The block's goals are:

1st Block – solve each task during the shops' opening hours;

2nd Block – complete the most relevant tasks first;

3th Block – group the tasks by physical proximity;

4th Block – find a faster way to complete all the tasks, using the different ways of travelling;

5th Block – use a limited budget;

6th Block – use a limited period of time for all tasks to be performed;

7th Block – find alternative solutions to unsolvable tasks (e.g., buy something in a closed shop).

Algorithm

During the rehabilitation program, the patients work independently, and the progress along levels and blocks is automatic and adapted to the users.

The success criteria change due to the diversity of evaluation block criteria. Moreover, the number of tasks per level is proportional to the level number. The basic rule that defines whether the patient is capable to advance to the next level is a combination between the number of tasks from the current level and the goal of the block. If the user schedules and performs 80% of those tasks according to the block's goal, the system allows the user to advance to the following level.

In order to adapt the game to the skills and learning rate of each user, the Virtual City has a strategy of progress along the blocks. When users perform three consecutive levels without interruptions, they immediately advance to the next block, even if they did not finish all the levels. This strategy avoids needless exercises, assuming they are too simple for the current user.

Architecture

The system is divided into three blocks (Fig. 3): User Interface, Game play and Database. The User Interface allows the interaction between the user and the game, using the mouse, keyboard or joystick. This block provides the interface with the game and also with other menus. The gameplay block manages the requests sent by the user and, if necessary, interacts with the database block. The database block has all the information about the mechanical part of the game and the users' personal and medical information.

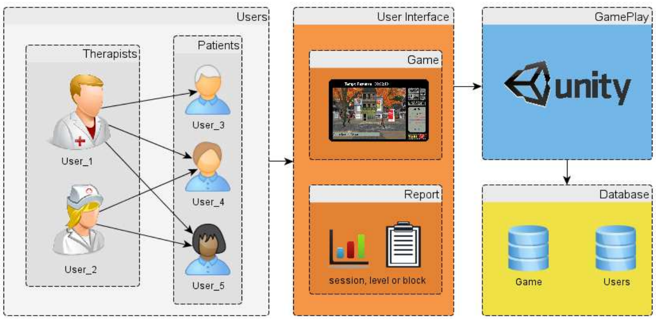

Figure 3- Architecture

The scenarios were modeled using the procedural modeling software, CityEngine. The city model was imported from OpenStreetMap (OSM) and the buildings and streets were generated by rules defined according to the information provided by the OSM file. The cities were exported as an FBX file and imported into Unity3D game engine. Unity3D is used for the game logic creation, for database access and to handle user requests. In the last stage of development, the project will be deployed as a web player.

The game's goals (Fig. 4) are stored in the database with all the level, block and task details. Each block has one or more evaluation criteria, depending on its position. The game has two kinds of users: therapists and patients. Therapists have total access to the results of their patients. However they cannot consult the charts of other therapists' patients. Patients have an account with restrict access, where they can practice or consult their previous results. Each patient (Fig. 4) has a session-log with all the information about their performance, such as session date, level's results, current level or which levels they gave up.

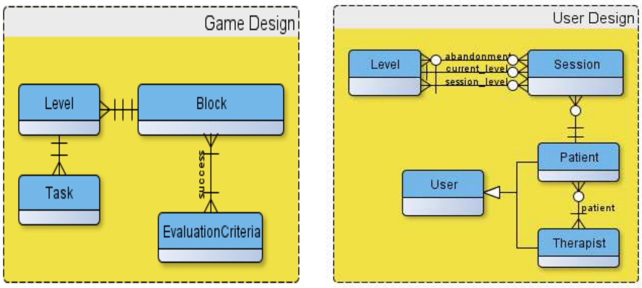

Figure 4- Game Design Model and User Design Model

Future Directions: Program Evaluation

After usability tests on the Virtual City, results in two intervention protocols will be assessed and compared: patients receiving no cognitive rehabilitation versus patients under no cognitive rehabilitation receiving CARP-VR: Virtual City.

The effects of each intervention protocol will be assessed through neuropsychological tests and functional magnetic resonance imaging (fMRI), applied at the beginning and end of each intervention. fMRI will allow the assessment of brain mechanisms involved in the process of cognitive rehabilitation. It is expected that the Virtual City intervention will lead to cognitive gains and to better generalization of acquired capacities to real-life activities than traditional interventions. It is also expected that results will remain at follow-up, three months after the end of the program, reflecting an amelioration of patients' functional independence and quality of life.

Following this evaluation, the Virtual City will be integrated with the other CARP-VR Programs, such as the previously mentioned House and Supermarket.

CONCLUSION

This paper sums up theoretical and practical difficulties concerning the neurocognitive rehabilitation of ABI patients, and stresses the need for innovative solutions. It also presents a brief reflection on technologies that could overcome the identified difficulties, namely SG and VR. Reflecting the team’s concern and interest in this thematic, the CARP-VR platform is presented. It aims to introduce daily problems and tasks to ABI patients, helping them to learn how to solve these problems in real life, by training in virtual environments. This project’s development process is organized in multiple phases, the Virtual City being currently under development. This program uses 3D models and VR.

The project’s progression follows the expectation to contribute to the implementation of SG and VR in the neurocognitive rehabilitation field, increasing the range of tools available to this end.

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Conclusão

Nas últimas décadas assistimos a um aumento considerável de ambientes em RV, desenvolvidos em especial na Educação, na Medicina e, mais recentemente, no domínio da Reabilitação. Contudo, a conceptualização, desenvolvimento e implementação de um programa de reabilitação neurocognitiva, particularmente com recurso à tecnologia de RV, permanece um processo exigente, complexo e com elevados custos associados ao equipamento e ao desenvolvimento. A estas dificuldades somam-se as da sua validação. Fatores como a diversidade individual na recuperação espontânea, a natureza, a localização e a magnitude da lesão, o tempo pós-ocorrência, a idade dos sujeitos, o nível de funcionamento pré-morbido, o consumo de substâncias, o nível sócio-educacional e a presença de perturbações psicológicas podem influenciar os resultados obtidos, dificultando as práticas de reabilitação e a investigação nesta área. A estas dificuldades somam-se as questões relacionadas com os princípios éticos que é preciso salvaguardar.

No trabalho apresentado nesta tese, a definição de critérios de inclusão e exclusão teve como objetivo providenciar algum controlo sobre estas variáveis. Segundo estes critérios reuniam condições para participar nos estudos sujeitos com LCA moderada, resultado de TCE ou de doenças neurológicas como o AVE, com idade compreendida entre os 18 e os 50 anos, mínimo de quatro meses pós ocorrência da LCA, ausência de consumo de substâncias, ausência de perturbações psicológicas severas, participação voluntária e assinatura do consentimento informado. Os estudos foram desenhados com respeitos pelos princípios consagrados na Declaração de Helsínquia e aprovados pelas comissões de ética locais.

Os programas de reabilitação neurocognitiva existentes continuam a refletir as dificuldades enunciadas. Particularmente na reabilitação das funções executivas, as limitações tecnológicas e metodológicas, decorrentes do exposto, são evidentes na ausência de destaque que esta função e as tarefas de reabilitação a ela dedicadas mereceram na literatura durante décadas. Assim, se da análise dos estudos revistos ressalta o facto da reconstrução da vida dos doentes com LCA se encontrar estreitamente relacionada com a reabilitação que lhes for proporcionada, sobressaem igualmente limitações dos programas convencionais e o potencial da RV na inovação e melhoria das práticas. A literatura sugere a necessidade de intervenções de elevada validade ecológica, promotoras de avaliações mais realistas e de competências provavelmente mais generalizáveis, porquanto treinadas em tarefas mais próximas do real, com maior envolvimento e interação dos doentes.

Apesar do entusiasmo inicial com a tecnologia RV, permanece atual a necessidade: (1) de ferramentas de intervenção inovadoras que potenciem a motivação para as tarefas, a reabilitação das funções cognitivas deficitárias e a generalização das competências adquiridas para contextos de vida real, e (2) de evidência empírica que assegure a eficácia das intervenções, por exemplo, através da análise dos seus efeitos na generalização e/ou nos mecanismos cerebrais envolvidos. Face a estas questões, novos métodos têm emergido, como os da neuroimagem funcional, frequentemente combinados com os métodos clássicos da neuropsicologia. Estes podem ser ferramentas úteis na validação dos programas desenvolvidos, providenciando dados comportamentais e funcionais associados ao desempenho nas tarefas propostas.

Com a realização deste projeto de doutoramento, além de disponibilizar novas ferramentas, procurámos contribuir para o debate em torno da reabilitação neurocognitiva e para a resposta às necessidades anteriormente enunciadas. Como resposta à primeira necessidade propusemos e validámos em termos de usabilidade o CARP-VR, como um Programa de reabilitação com recurso à tecnologia de RV, esperando contribuir para melhorar os défices cognitivos, com especial relevo os associados às funções executivas, minimizar o seu impacto na readaptação à vida real e promover a integração ambiental, expressa numa maior independência funcional e em medidas de qualidade de vida.

Como resposta à segunda necessidade, procurámos reunir evidência empírica acerca dos efeitos dos Programas de RV, pelo que encetámos um conjunto de estudos, alguns já concluídos e de que adiante faremos uma apresentação sumária dos resultados, outros em curso. Nestes foram consideradas medidas de avaliação da satisfação, da motivação para participar na reabilitação, da funcionalidade e testes de avaliação neuropsicológica. Ainda, uma técnica de neuroimagem, a ressonância magnética funcional (RMf), aplicada ao estudo dos mecanismos cerebrais envolvidos em tarefas relacionadas com as funções executivas. Esta técnica por ser pouco invasiva, além das suas reconhecidas aplicações clínicas, começou nas últimas décadas a ser utilizada no domínio da investigação, permitido o mapeamento das áreas cerebrais envolvidas nos diferentes processos cognitivos em indivíduos saudáveis, pelo que decidimos acerca da sua utilização. Porém, esta não está isenta de dificuldades, das quais realçamos a seleção adequada da tarefa específica às áreas a ativar ou às operações cognitivas a estudar. Com os artigos de neuroimagem visámos contribuir com a proposta de novos paradigmas que permitissem estudar o efeito da RV. Mais concretamente, o exercido por uma das suas características distintivas - a tridimensionalidade -, esperando aumentar a compreensão das suas vantagens. Esta característica recente, potenciadora da sensação de presença nos ambientes RV, está a assumir uma importância cada vez maior nos paradigmas metodológicos que importa perceber melhor. Por exemplo, na compreensão do efeito que pode exercer na resposta cerebral a estímulos emocionais, por comparação com a sua visualização bidimensional. Considerando a relevância do estudo do processamento da informação emocional, cremos que o controlo da valência emocional dos ambientes virtuais é um objeto de estudo que deve merecer maior atenção na conceção de programas de reabilitação. Particularmente, se tivermos em atenção que os estímulos significativos a que os sujeitos são expostos, despoletam nele uma dimensão cognitiva, vivencial e expressiva, frequentemente confundidas na literatura, mas que são distintas. Com o propósito de promover investigação nesta área, concebemos e validámos dois paradigmas que propõem tarefas para avaliar o controlo atencional e inibitório e a memória de trabalho respetivamente, com controlo da valência emocional. Estas funções foram escolhidas pela estreita relação que apresentam com as funções executivas, que pretendemos continuar a estudar em populações clínicas.

Em jeito de síntese, para além das inovações tecnológicas na reabilitação neurocognitiva, procurámos introduzir inovações metodológicas no seu estudo. Os trabalhos realizados de cujos objetivos específicos e produtos científicos demos conta, foram organizados em doze estudos interdependentes, de que a seguir se faz uma retrospetiva: (1) estudo da aplicação da RV à reabilitação e análise das evidências sobre a sua eficácia, através de uma revisão sistemática da literatura (Artigo 1); (2) estudo da importância das funções executivas na reintegração da pessoa com LCA, do modo como é conceptualizado esse funcionamento e de quais as práticas atuais de intervenção e investigação sobre este objeto, com a mesma metodologia do estudo anterior (Artigo 2); (3) descrição do processo de desenvolvimento do CARP-VR, dando realce à importância da integração teoria-prática, e à estruturação do processo de desenvolvimento deste tipo de ferramentas em etapas organizadoras dos procedimentos e da participação diferenciada dos profissionais envolvidos (Artigos 3 a 5); (4) apresentação da versão final do Programa, com uma descrição detalhada das suas funcionalidades (Artigo 6 e Anexo I); (5) apresentação dos principais resultados obtidos com o CARP-VR em termos de desempenho e satisfação com a utilização do programa, controlando o modo de visualização, seguida dos resultados em termos de usabilidade e da promoção da motivação para participar na reabilitação (Artigo 7); (6) estudo do efeito da tridimensionalidade no funcionamento cerebral, induzido por estímulos de conteúdo emocional, com diferentes valências (agradável, desagradável, neutra), em áreas específicas do processamento emocional (Artigo 8); e (7) do processamento visual, além do emocional (Artigo 9); ainda no domínio da neuroimagem funcional, proposta de dois paradigmas (8) para o estudo do controlo atencional e inibitório (Artigo 10); e (9) para o estudo da memória de trabalho (Artigo 11); por último (10), é documentado o trabalho em curso para dar continuidade ao desenvolvimento do CARP-VR (Artigo 12 e Anexo II e III).

Tomando como referência esta organização, genericamente estruturada em *Enquadramento Teórico* (Artigos 1 e 2), *Desenvolvimento, Implementação e Avaliação* do *Computer-Assisted Rehabilitation Program - Virtual Reality* (CARP-VR) (Artigos 3 a 7), Desenho e Validação de Paradigmas Experimentais (Artigos 8 a 11) e *Trabalhos em Curso* (Artigo 12) apresentamos a seguir as metodologias, as conclusões dos estudos realizados e as suas implicações.

Ao longo desta tese de doutoramento procurámos desenvolver competências em diferentes metodologias de investigação. Nos estudos 1 e 2 em que se pretendia realizar o enquadramento teórico da temática, ao nível da RV e das funções executivas, respetivamente, foi utilizada uma metodologia qualitativa que contrasta com as por nós utilizadas subsequentemente, por exemplo, nos estudos de neuroimagem. Esta metodologia qualitativa pareceu-nos adequada à identificação das categorias organizadoras das temáticas em estudo e das suas relações, tal como emergem da literatura. Ao agir assim esperámos ainda reduzir a influência dos quadros teóricos de referência dos investigadores, na medida em que se realizaram análises indutivas, portanto, sem categorias prévias. Num dos estudos procurámos conciliar esta abordagem com uma posterior análise quantitativa que favorecesse um melhor entendimento da relevância de cada uma das categorias identificadas. Visámos, deste modo, contribuir para uma compreensão mais real e integradora das temáticas em questão, procurando simultaneamente um formato de apresentação das revisões, mais compatível com o que é atualmente recomendado em termos de redação de teses de doutoramento, a sua organização em artigos. Estes refletem, assim, uma abordagem que se espera rigorosa e detalhada, no sentido de tornar o processo reprodutível.

Mais concretamente, o Estudo 1 focou-se sobre trabalhos científicos indexados, até novembro de 2010, na base de dados ISI Web of Knowledge. Os trabalhos incluídos foram analisados por dois investigadores independentes no programa NVivo 9 e o modelo desenvolvido foi posteriormente aplicado à recodificação do material em análise. Foram identificados 963 artigos, dos quais, aplicados os critérios de exclusão, 288 títulos e resumos foram analisados. O modelo desenvolvido indica, como categorias centrais da bibliografia: *Tipo de Artigo (Empírico; Teórico); Contextualização do Projeto; Tipo de Abordagem (Tecnologia Assistiva; Realidade Aumentada; Abordagens Tradicionais; Realidade Virtual)*. Esta última categoria (RV) foi decomposta de forma exaustiva para documentação da sua aplicabilidade, efeitos e tendências futuras. Como vantagens da RV, surgem: a possibilidade da sua aplicação a uma diversidade de domínios, funções cognitivas, comportamentos, doenças neurológicas e incapacidades físicas; as suas características e respetivas consequências; e a possibilidade de superar limitações das intervenções tradicionais. Do lado das limitações aparecem discutidos: os efeitos secundários da RV, as causas das limitações e precauções sugeridas. Os resultados evidenciam tendências promissoras acerca da utilização da tecnologia de RV no domínio da reabilitação, com implicações para a forma como será realizada no futuro. Sugerem ainda a necessidade de dar continuidade aos trabalhos que procuram avaliar a aplicabilidade da RV na reabilitação em geral e na reabilitação (neuro)cognitiva em particular.

No Estudo 2 a revisão da literatura foi realizada em artigos científicos indexados, até abril de 2011, no ISI Web of Knowledge, com recurso ao NVivo9. Dois codificadores independentes realizaram a análise indutiva, e construíram um modelo hierárquico com categorias e subcategorias de temas emergentes da literatura. O modelo desenvolvido foi utilizado pelos mesmos investigadores de modo independente na recodificação do material. O processo foi validado por um juiz. Aplicados os critérios de exclusão, de 187 títulos e resumos foram analisados 91. Os resultados foram estruturados em oito categorias principais, duas referentes ao *Tipo de Artigo* e ao *Domínio Científico* e seis referentes a temas emergentes: *Modelos do Sistema Nervoso Central, Diagnóstico, População, Avaliação, Intervenção* e *Modelos Teóricos*. As principais conclusões evidenciam tendências promissoras na avaliação e na reabilitação, e potenciais implicações nas intervenções atuais e nas investigações futuras.

No Estudo 3 pretendemos relançar o debate em torno do desenvolvimento de programas de reabilitação neurocognitiva, explorando desafios e propondo soluções. Numa era em que a tecnologia sofreu um desenvolvimento exponencial, importa recolher dela os benefícios, controlando a sedução em fazer dela o foco principal. Como já referido, noutros momentos ao longo desta tese, tal pode implicar um equilíbrio delicado entre a teoria e a prática que é preciso conseguir e promover, por exemplo, através da proposta de modelos organizadores do processo do desenvolvimento destes programas. Nesse sentido apresentámos a proposta do processo de desenvolvimento de um programa de reabilitação, estruturado em 11 tarefas a partir da revisão da literatura, da consulta de especialistas e da incorporação de alterações decorrentes do refinamento do próprio processo. Este reflete uma forte integração teoria-prática e a análise crítica dos resultados, ambas aqui consideradas por serem na nossa perspetiva nucleares. Na nossa proposta o desenvolvimento do Programa de Reabilitação em RV deve começar com a Revisão Teórica e Reflexão acerca das Práticas (Tarefa 1), de acordo com os passos 1 a 4 do Modelo de Sohlberg e Mateer (1989), ponto de partida para o Desenho conceptual (Tarefa 2). Na Tarefa 2, de acordo com os passos 5 e 6 do Modelo de Sohlberg & Mateer (1989), os psicólogos membros da equipa multidisciplinar apresentam os requisitos do programa (designadamente, quais os ambientes virtuais, as atividades a desenvolver em cada ambiente, o número de níveis de dificuldade de cada ambiente) tendo em conta a especificidade da população estudada, e os engenheiros da equipa contribuem com sugestões para a operacionalização desses requisitos. Para o Desenvolvimento da Aplicação de Interação (Tarefa 3), é especificado o modo de interação dos doentes com o programa, baseado no conhecimento dos psicólogos acerca das características destes doentes e nas soluções técnicas por parte da Engenharia. Para o Desenvolvimento dos Ambientes Virtuais (Tarefa 4), são especificados os referidos ambientes. É ainda especificada a metodologia dos estudos piloto e experimental, a realizar, e os eventos de divulgação do processo e do(s) produto(s) (Tarefas 7 a 11). Por último, são sugeridos critérios a considerar na seleção de um programa de reabilitação. Por ser um artigo que surgiu da confluência de áreas de especialidade clínica e tecnológica, esperámos que da sua realização pudessem resultar mais informação e orientações úteis aos profissionais na área da reabilitação cognitiva, no sentido de estimular o seu interesse pelo desenvolvimento de ferramentas de reabilitação e/ou facilitar a seleção entre as que existem no mercado, e aos profissionais da área da Engenharia Computacional, para que possam reunir mais informação acerca das reais necessidades dos futuros utilizadores dos produtos que desenvolvem.

Nos Artigos 4 e 5 visámos a apresentação do projeto inicial do CARP-VR à comunidade científica. Destes resultou uma clarificação de planos e métodos, da arquitetura do Programa de reabilitação e da(s) modalidade(s) de interação “homem-máquina”, fruto do *feedback* e sugestões recolhidas que favoreceram a sua conceção .

No Artigo 6 teve-se como objetivo apresentar o CARP-VR na sua versão final. Das características gerais do CARP-VR destacamos ser constituído por dois ambientes distintos. O primeiro, chamado de treino, consiste numa casa. O segundo, designado de reabilitação, consiste num parque de estacionamento e num supermercado. No ambiente de treino, os doentes podem explorar três cenários diferentes: Cenário 1 - sala de arrumos; Cenário 2 - sala de jantar; Cenário 3 – quarto. Nestes cenários, os indivíduos têm de resolver diferentes tarefas de complexidade crescente, mas reduzida, por ser um ambiente de formação acerca da utilização da tecnologia. As competências treinadas são: a classificação, o reconhecimento e a resolução de problemas. A conceção deste primeiro ambiente teve como objetivos: (1) ajudar a decidir o *hardware*, o *software* e o sistema de visualização a ser implementado no CARP-VR final, (2) avaliar o grau de satisfação com a sua utilização e, numa fase posterior já como parte do CARP-VR final, permitir aos doentes experimentar a tecnologia de RV e a navegação antes de iniciar a reabilitação propriamente dita. O Programa final apresenta níveis pré-definidos e a possibilidade destes serem construídos pelos próprios terapeutas, sem necessidade de conhecimentos de programação, a partir da variação de um conjunto de parâmetros como: Lista de Produtos (Visível ou Não), Formato de Lista (Auditiva ou Visual); Instruções (Sim (S)/Não (N)); Início Retardado·(S/N); Repetição (S/N); Erro Permitido (S/N); Correções (S/N), Número de Produtos a serem comprados; Número de Seções; Preços dos Produtos (S/N); Visualização do Mini-Mapa do supermercado (S/N), Tempo Limite (S/N); "Palavras Mágicas", para o treino de automonitorização e autoinstrução; Tempo Limite (S/N); Relógio (S/N) e requisitos especiais (envolvendo resolução de problemas, cf. Anexo I). Estes podem ser combinados para aumentar o grau de dificuldade das tarefas ao longo do programa e de modo contingente ao desempenho do doente. Neste artigo foram ainda apresentadas a arquitetura do sistema e as especificações técnicas referentes aos editores de mapas e níveis e ao armazenamento dos resultados do desempenho. Como implicações, com o desenvolvimento do CARP-VR esperamos ter contribuído para o avanço do estudo científico da tecnologia de RV e das suas aplicações ao domínio da reabilitação, aumentando o número de soluções disponíveis. Por outro lado, uma abordagem multidisciplinar no seu desenvolvimento ambicionou a conceção de um programa que se enquadre na atual conjuntura económica de contenção e otimização de recursos, e possa desempenhar um papel na adaptação dos serviços às necessidades dos doentes, maximizando o seu acesso à reabilitação e à formação profissional; em última instância, o seu retorno ou acesso ao emprego, em muitos casos, uma condição necessária para retornar à sua vida.

No Artigo 7 o objetivo foi explorar a eficácia do CARP-VR, nos seus diferentes ambientes e modos de visualização, partindo de uma análise comportamental. Este propósito foi realizado através de três estudos exploratórios. Os resultados do estudo com a utilização do ambiente de treino "casa virtual", e com o modo de visualização 2D evidenciam uma melhoria no tempo necessário (em média) para executar as tarefas solicitadas. Da primeira para uma segunda administração das tarefas do programa de treino observou-se uma redução do tempo necessário à sua realização e do número de erros. O estudo também mostra a influência da tecnologia RV na motivação para a tarefa, tendo sido observado o envolvimento na realização das tarefas, documentado pela persistência na tarefa e pelas verbalizações positivas acerca do mesmo. No inquérito por questionário os doentes revelaram desejo de continuar a realizar tarefas similares. No estudo 2 deste artigo, foram estudadas as mesmas variáveis mas o modo de visualização aqui foi 3D. Ao compararmos com o modo de visualização em 2D, não se registou uma melhoria significativa no tempo necessário para completar as tarefas. No entanto, o número de erros foi menor no modo de visualização em 3D. Em relação ao potencial da tecnologia de RV na promoção do envolvimento os resultados foram similares nos dois modos de visualização (2D e 3D). Além disso, nos dois casos surgiram respostas equivalentes e positivas ao questionário sobre a satisfação. As principais dificuldades identificadas pelos doentes em relação ao Programa proposto consistiram na utilização simultânea do rato e do teclado para navegar, dadas as suas limitações físicas. A principal vantagem apontada à visualização em 3D foi a maior dimensão dos objetos e ambientes, resultante do sistema de projeção utilizado. Além disso, o interesse manifestado em participar em futuros estudos foi superior com a utilização do 3D. Por último, no estudo 3 já com o ambiente “Supermercado”, foi avaliada a usabilidade do sistema. Todos os participantes obtiveram pontuações acima do ponto médio da escala, emprestando apoio à usabilidade do programa. No entanto, os resultados devem ser interpretados com cautela, particularmente no que diz respeito à influência dos itens 4 e 10 na pontuação global. As respostas a estes itens não traduzem necessariamente o desempenho dos sujeitos no Programa, mas as suas perceções pessoais dos seus défices e da sua autoeficácia. Dadas as patologias em questão, alguma falta de correspondência com a realidade é esperada nesta população. Pode haver uma tendência para sobrestimar ou subestimar as capacidade reais, que este Programa pode ajudar a corrigir pelo confronto com a evidência dos resultados obtidos e/ou com a promoção de sucesso otimizador de uma visão de si mais positiva, de acordo com as especificidades de cada caso. Os participantes no estudo reconheceram ainda a relevância do Programa na motivação para participar no processo de reabilitação. Todos os participantes atribuíram uma pontuação superior a três (ponto médio da escala) a este item. Resumidamente os resultados nos estudos-piloto com doentes com LCA são promissores, apoiando a usabilidade do Programa e demostrando a sua relevância na motivação para participar no processo de reabilitação, o que também reflete a sua satisfação com ele. A realização deste estudo permitiu-nos confirmar o potencial da tecnologia, sinalizado na literatura em diversas áreas da clínica, sugerindo a sua inclusão nos programas de reabilitação. Contribuiu ainda para motivar novos desenvolvimentos.

Os quatro estudos seguintes, de neuroimagem funcional, visaram aumentar a compreensão dos efeitos da RV no funcionamento cerebral, e promover o conhecimento acerca do seu modo de atuação. Concretamente, no Artigo 8 comparámos a diferença entre a visualização 3D e 2D de estímulos visuais, organizados em ambientes virtuais de diferentes valências (agradável, desagradável, neutra) e o seu efeito sobre a atividade cerebral de áreas relacionadas com a emoção. Justificam a inclusão desta variável considerarmos que apesar das soluções tecnológicas existentes serem cada vez mais diversas, acessíveis e de maior qualidade, as aplicações científicas e clínicas da RV e o seu desenvolvimento implicam muito mais do que a disponibilidade da tecnologia. Verifica-se, igualmente, a necessidade de inclusão de novas variáveis nos estudos acerca dos efeitos desta tecnologia no indivíduo, designadamente na indução da emoção, aspeto em que o recurso à RV parece ser particularmente vantajoso. Diferentes autores têm demonstrado de forma clara o papel central que a emoção desempenha em múltiplos aspetos da regulação do comportamento, em populações saudáveis e clínicas, designadamente com LCA. A tecnologia RV, ao eliminar a passividade do sujeito perante a visualização de imagens, pela imersão, interação e envolvimento, pode contribuir para o aumento da intensidade da resposta emocional, aproximando-a mais das contingências da vida real. Justifica-se, assim, o interesse recente na RV também para a compreensão dos fenómenos emocionais.

Os resultados mostram-nos que os estímulos desagradáveis e neutros ativam mais a amígdala direita quando apresentados em 3D, em comparação com 2D. Este resultado sugere que o maior realismo e o aumento da sensação de presença associada aos estímulos 3D pode regular a resposta da amígdala. O facto de se verificar a tendência, ainda que com uma significância marginal, para os cenários negativos induzirem uma ativação superior aos positivos pode ser interpretado à luz da biopsicologia das emoções. Já uma ativação superior nos cenários neutros é de mais difícil explicação e importa verificar a sua reprodução em estudos futuros. Voltando aos cenários desagradáveis, tem sido demonstrado que a capacidade de processar estímulos ameaçadores ou de risco é da ordem dos milissegundos, sendo este tempo suficiente para provocar uma resposta emocional. Relembramos, por exemplo, a presença de uma cobra, como um dos objetos do cenário desagradável que, tal como outros estímulos do cenário, representa um medo ancestral. De facto, a literatura advoga a manutenção da via rápida do processamento emocional em termos evolutivos, provavelmente como estratégia de preservação da espécie e promotora da adaptação ao meio. Apesar das contribuições filogenéticas, que permitem explicar a importância de condições desagradáveis em termos evolutivos, devemos ter presente que estas podem ser modificáveis por fatores ambientais que aumentem ou diminuam essa influência. Assim, pela aplicação dos princípios de condicionamento operante e a ação de estímulos apetitivos (reforçadores) ou aversivos (punitivos), pode ser criada uma predisposição para a ação que pode variar entre aproximação/apetite e evitamento/aversão, sendo reconhecido o papel dos estímulos aversivos na modificação do comportamento. Por outro lado, a relevância das emoções negativas face às positivas reflete-se ainda, por exemplo, na proposta teórica de Ekman, que no seu estudo de identificação das expressões faciais de emoções primárias propõe seis emoções negativas (Raiva, Tristeza, Medo, Nojo, Surpresa, Desprezo) por oposição a uma única positiva (Alegria).

No estudo 9 o nosso objetivo foi explorar o substrato neuronal associado ao processamento de estímulos visuais tridimensionais, controlando o efeito de valência emocional. Verificou-se um efeito de interação entre a valência emocional e tipo de visualização em áreas corticais e subcorticais responsáveis pelo processamento emocional, além da ativação de componentes do sistema límbico. Estes resultados são consistentes com a literatura, onde investigação e modelos neurobiológicos recentes reconhecem o papel destas estruturas no processamento emocional. A análise da direção dos efeitos entre a valência emocional (agradável, desagradável e neutra) e o tipo de visualização (2D, 3D) evidenciou, o efeito esperado (valência desagradável > agradável > neutra) para o tipo de visualização 2D, mas apenas a valência emocional agradável induziu maior activação do que a neutra com a visualização em 3D. Por sua vez, a análise da direção dos efeitos entre tipo de visualização e valência emocional revelou que a visualização em 3D produziu maior ativação do que a 2D para a valência agradável, mas o efeito contrário na valência neutra, sinalizando a necessidade de estudos adicionais. Estudámos ainda o efeito destas variáveis (valência emocional e tipo de visualização) de modo independente. Como efeito principal da valência emocional verificámos o conhecido efeito induzido por emoções negativas, como o cenário desagradável a produzir maior activação do que o agradável e/ou o neutro em todas as regiões do cérebro ativadas. O mesmo se verificou com o cenário agradável a produzir maior ativação do que o neutro em algumas das regiões cerebrais. Estes resultados parecem consistentes com o já explanado anteriormente, relativo ao artigo 8, no que concerne ao papel das emoções negativas. Por último, quando analisámos os resultados do efeito principal do tipo de visualização (independentemente da valência emocional), o 3D consistentemente induziu maior activação do que o 2D, em todas as regiões cerebrais ativadas. Este estudo e os resultados obtidos parecem contribuir para esclarecer os mecanismos cerebrais envolvidos no processamento de estímulos tridimensionais, demonstrando a sua importância, porquanto mais próximos dos reais, e a sua interação com a valência emocional dos cenários, sugerindo não poder ser considerada uma variável negligenciável.

No estudo 10 o objetivo foi o de apresentar um paradigma, baseado no Williams Inhibition Test (WIT), para estudar o controlo atencional e inibitório e o correspondente substrato neuroanatómico. Embora investigações anteriores tenham realizado estudos de neuroimagem com paradigmas experimentais baseados nas tarefas de Stroop e de Simon, que apresentam algumas semelhanças com o WIT, este último é mais exigente, e ainda não há evidência a partir de neuroimagem das áreas ativadas durante o seu desempenho, nem de que ele permite a discriminação dos desempenhos entre populações saudáveis e clínicas. Definimos como regiões de interesse o córtice pré-frontal dorsolateral (Áreas de Brodmann [BA] 9/46), o córtice pré-frontal inferior (BA 44), o córtice cingulado anterior (BA 32), e o posterior (BA 6). Comparámos ainda os dados comportamentais (acertos, erros, tempos de reação) dos participantes saudáveis com os de doentes com LCA. Os resultados mostram o envolvimento das regiões definidas e indicam que o WIT é sensível a lesões cerebrais, sugerindo que o paradigma proposto pode ser utilizado como metodologia de investigação em estudos comportamentais e de neuroimagem das componentes atencionais e inibitórias das funções executivas.

O estudo 11 propôs e validou um paradigma de fMRI utilizando uma adaptação de uma tarefa de *n-back*, com estímulos não verbais. Neste foi ainda estudado se a tarefa proposta permitia discriminar entre indivíduos saudáveis e com LCA, participantes num programa de reabilitação. Nos participantes saudáveis os dados revelam um aumento do sinal BOLD numa rede de áreas cerebrais distribuídas pelas vias visuais dorsal e ventral, envolvidas no processamento de informação visuoespacial, em particular nas áreas especializadas para a memória de trabalho visual, e pelas áreas de monitorização e manipulação da informação. No que respeita à capacidade da tarefa proposta discriminar entre os participantes saudáveis e com LCA, avaliada através de dados comportamentais, os participantes saudáveis mostraram o padrão previsto de mais acertos, menos omissões, uma tendência para menos falsos alarmes, mais respostas autocorrigidas e tempos de reação inferiores. Os resultados sugerem que essa tarefa pode ser utilizada como parte da metodologia de investigação em estudos comportamentais e de neuroimagem. Além de fornecer dados normativos, este estudo também apresenta um critério de validação através de um grupo clínico.

No estudo 12 tivemos como objetivo apresentar o protótipo da Cidade Virtual, concebida como uma extensão do CARP-VR. Conscientes de que aquilo que aqui propusemos é um processo, mais do que uma tarefa que se esgote na conclusão deste doutoramento, desenvolvemos esforços que permitissem dar continuidade ao Programa. São exemplo disso, encontrarem-se em curso duas dissertações de mestrado na FEUP, das quais a autora desta tese é coorientadora (Cf. Artigo 12, Anexo II e III). Estes trabalhos visam aumentar os ambientes virtuais disponíveis no CARP-VR e as funcionalidades do Programa, ainda a integração dos diversos ambientes desenvolvidos e sua disponibilização numa plataforma que permitirá a participação à distância (Anexo II e III).

Ao terminar a apresentação dos estudos empíricos devemos realçar como limitações os resultados das estatísticas aplicadas nem sempre terem sido os mais robustos, dada a dimensão reduzida dos grupos, o que limita a possibilidade da sua generalização. Grupos maiores seriam também desejáveis nos casos em que considerámos que as tarefas propostas permitiam obter dados normativos relevantes. Por outro lado, a dimensão dos grupos foi uma variável que esteve fora do controlo da equipa, dado os procedimentos associados à sua participação envolverem elevados custos, pouco compatíveis com o financiamento de que dispúnhamos ou com o mecenato científico que conseguimos. Tal não foi impeditivo deste trabalho e se com ele conseguimos resultados relevantes, estes provavelmente advogarão a respeito da qualidade das tarefas experimentais propostas. Foi igualmente difícil controlar o tempo associado ao desenvolvimento dos materiais, em muitos casos dependente de trabalho voluntário, e lidar com o custo da tecnologia envolvida.

Consideramos positivo a diversidade de metodologias aplicada e o trabalho multi e interdisciplinar conseguido. Em termos de procedimentos, parece-nos merecer destaque termos tido o cuidado de que o processo de desenvolvimento das ferramentas ocorresse em estreito diálogo com os principais beneficiários da sua utilização, os doentes com LCA e os profissionais desta área. Estes contribuíram com sugestões para a sua a melhoria e validação. Foram ainda recolhidos dados que nos permitem dar continuidade à investigação aqui realizada acerca da eficácia do CARP-VR, mais concretamente estudar a correlação entre os resultados obtidos por sujeitos com LCA em 14 níveis do Programa, representativos dos múltiplos patamares (conjunto de níveis do mesmo tipo, mas de complexidade crescente) e das funções cognitivas em que visamos intervir, com os resultados da avaliação neuropsicológica. Encontra-se também a decorrer um estudo piloto, com a duração de três meses, e duas sessões semanais de 60 minutos. Neste serão utilizadas como medidas de avaliação da eficácia, instrumentos de avaliação da funcionalidade, pré e pós-teste, além da avaliação neuropsicológica, e entrevistas semiestruturadas, de modo a explorar a generalização das capacidades adquiridas para atividades da vida real (cf. Anexo I). Depois destes estudos consideramos ter reunidas as condições à implementação do CARP-VR junto de uma amostra alargada de participantes voluntários, com LCA, abrindo portas a uma nova fase da investigação. Da metodologia prevista para esta fase damos conta no Anexo I, secção “Planificação da Avaliação Futura do Programa”.

Queremos ainda referir, como parte dos trabalhos em curso/futuros, o envolvimento da equipa num projeto que tem como objetivos (1) avaliar o impacto do programa holístico de reabilitação neuropsicológica (PHRN) implementado no CRPG em variáveis como a qualidade de vida, a estabilidade emocional, o funcionamento cognitivo geral e a funcionalidade e (2) a aferição para Português Europeu de um questionário de avaliação da Qualidade de Vida específico para pessoas com LCA*, o Quality Of Live after Brain Injury* (QOLIBRI**,** von Steinbuchel et al., 2010; Truelle et al., 2010), na versão portuguesa (Guerreiro et al., 1994). Este projeto visa contribuir na resposta à necessidade, já anteriormente reportada e norteadora desta tese, de se saber quais os fatores da intervenção e as características dos doentes que otimizam os resultados da reabilitação, ultrapassando a questão de se investigar se esta é ou não eficaz.

Retomando a questão do estudo da emoção em programas de reabilitação, propomo-nos ainda investigar as diferenças nas respostas fisiológicas e cerebrais a estímulos emocionais por oferecem dados objetivos sobre o processamento da informação emocional. De entre os estímulos emocionais, as faces são importantes estímulos sociais em humanos. Particularmente a capacidade de reconhecer emoções em expressões faciais é fundamental na comunicação e na interação social, pelo que merecerão o nosso interesse. Pretendemos, igualmente, continuar a estudar se as respostas emocionais podem ser modeladas pela tridimensionalidade dos estímulos, visto essa característica potenciar a sensação de presença no sujeito. Este projecto visa, assim, testar o efeito de estímulos de maior realismo na indução de emoções em ambiente laboratorial controlado, onde são possíveis medidas fisiológicas, neurofisiológicas e neuroimagiológicas em tempo real.

Para a sua concretização encontramo-nos a validar a *Radboud Faces Database* (RaFD) com adultos (Langner et al., 2010). Os melhores estímulos em termos de categoria emocional serão posteriormente utilizados em duas tarefas experimentais – uma de identificação e outra de discriminação de categorias emocionais primárias - com registo poligráfico simultâneo (condutância eléctrica da pele e ritmo cardíaco) e registo do tempo de reação, manipulando o formato de apresentação (2D, 3D). Numa fase posterior, o efeito da categoria e da tridimensionalidade na atividade/respostas cerebrais será testado através de um estudo neurofisiológico e de neuroimagiologia funcional. Este estudo com recurso a medidas comportamentais e biológicas objetivas não só contribuirá para a compreensão dos mecanismos cerebrais envolvidos no processamento de emoções primárias, como ajudará à clarificação dos contributos da realidade virtual para a investigação das emoções e das suas aplicações clínicas.

Apesar das limitações anteriormente enunciadas, e que pretendemos colmatar nos trabalhos em curso/futuros, esperamos ter dado um contributo válido ao abordar uma temática atual, de reconhecido interesse científico e social, a reabilitação neurocognitiva de sujeitos com LCA. Particularmente, ao colaborar na resposta à necessidade de ferramentas de intervenção inovadoras e na procura de evidência empírica que assegure a eficácia das intervenções e a compreensão dos seus mecanismos de atuação.

Ao terminar, resta-nos referir que se a atividade descrita nesta tese se reveste, como não podia deixar de ser, de desafio, os resultados são compensadores. Partilhamos da perspetiva de Thomas Edison, quando questionado como se sentia depois de ter fracassado incontáveis vezes na tentativa de fabricar uma lâmpada, «Eu nunca fracassei, muito pelo contrário. Consegui descobrir, com grande êxito, milhares de procedimentos de como não fabricar uma lâmpada». Para nós isto só pôde ser fonte de aprendizagem e crescimento.

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APÊNDICES

APÊNDICE I - Records Analyzed Organized Chronologically

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ANEXOS[19]

[19] Entregues em separado.

ANEXO I - Programa CARP-VR
Computer-Assisted Rehabilitation Program – Virtual Reality

ANEXO II - Jogo Sério para Reabilitação Neurocognitiva: Cidade Virtual Projeto

ANEXO III – Jogo Sério para Reabilitação Neurocognitiva: Cidade Virtual Estado Atual